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(54) UTILISATION DE DERIVES DE 1,2-BENZISOTHIAZOL 2-SUBSTITUES ET DE DERIVES DE TETRAHYDROPYRIDOPYRIMIDINONE 3-SUBSTITUES POUR ASSURER LA PROPHYLAXIE ET LE TRAITEMENT DE L'ISCHEMIE CEREBRALE

(54) UTILISATION OF 2-SUBSTITUTED 1,2-BENZISOTHIAZOLE DERIVATIVES AND 3-SUBSTITUTED TETRAHYDROPYRIDOPYRIMIDINONE DERIVATIVES FOR THE PROPHYLAXIS AND THERAPY OF CEREBRAL ISCHAEMIA

(57)

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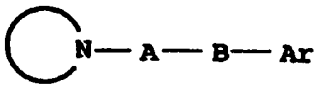


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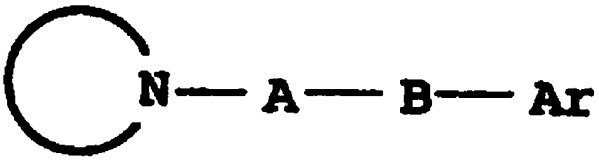


(I)

(57) Abrégé/Abstract:
The invention relates to the utilisation of compounds of formula (I) wherein the substituents have the meanings given in the description. The invention also relates to the salts thereof comprising pharmacologically compatible acids for producing medicaments for the prophylaxis and therapy of cerebral ischaemia and strokes.

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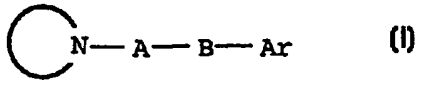
(54) Title: UTILISATION OF 2-SUBSTITUTED 1,2-BENZISOTHIAZOLE DERIVATIVES AND 3-SUBSTITUTED TETRAHYDROPYRIDOPYRIMIDINONE DERIVATIVES FOR THE PROPHYLAXIS AND THERAPY OF CEREBRAL ISCHAEMIA

(54) Bezeichnung: VERWENDUNG VON 2-SUBSTITUIERTEN 1,2-BENZISOTHIAZOL-DERIVATEN UND VON 3-SUBSTITUIERTEN TETRAHYDROPYRIDOPYRIMIDINON-DERIVATEN ZUR PROPHYLAXE UND THERAPIE DER ZEREBRALEN ISCHÄMIE

(57) Abstract

The invention relates to the utilisation of compounds of formula (I) wherein the substituents have the meanings given in the description. The invention also relates to the salts thereof comprising pharmacologically compatible acids for producing medicaments for the prophylaxis and therapy of cerebral ischaemia and strokes.



(I)

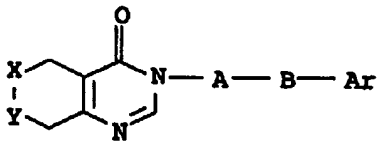
(57) Zusammenfassung

Verwendung von Verbindungen der Formel (I), worin die Substituenten die in der Beschreibung angegebene Bedeutung besitzen, sowie deren Salze mit pharmakologisch verträglichen Säuren zur Herstellung von Medikamenten zur Prophylaxe und Therapie von zerebraler Ischämie und Schlaganfall.

# UTILISATION OF 2-SUBSTITUTED 1,2-BENZISOTHIAZOLE DERIVATIVES AND 3-SUBSTITUTED TETRAHYDROPYRIDOPYRIMIDINONE DERIVATIVES FOR THE PROPHYLAXIS AND THERAPY OF CEREBRAL ISCHAEMIA

The invention relates to the use of compounds of the formula I for the prophylaxis and therapy of cerebral ischemia.

DE 19747063.7 describes 3-substituted tetrahydropyridopyrimidinone derivatives of the formula I



(I),

in which

one of the two radicals X, Y is $CH_2$ and the other is $NR^1$,

$R^1$ is hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, $CO-(C_{1-4})$-alkyl, $CO_2tBu$, CO-aryl or a phenyl-$C_1$-$C_4$-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

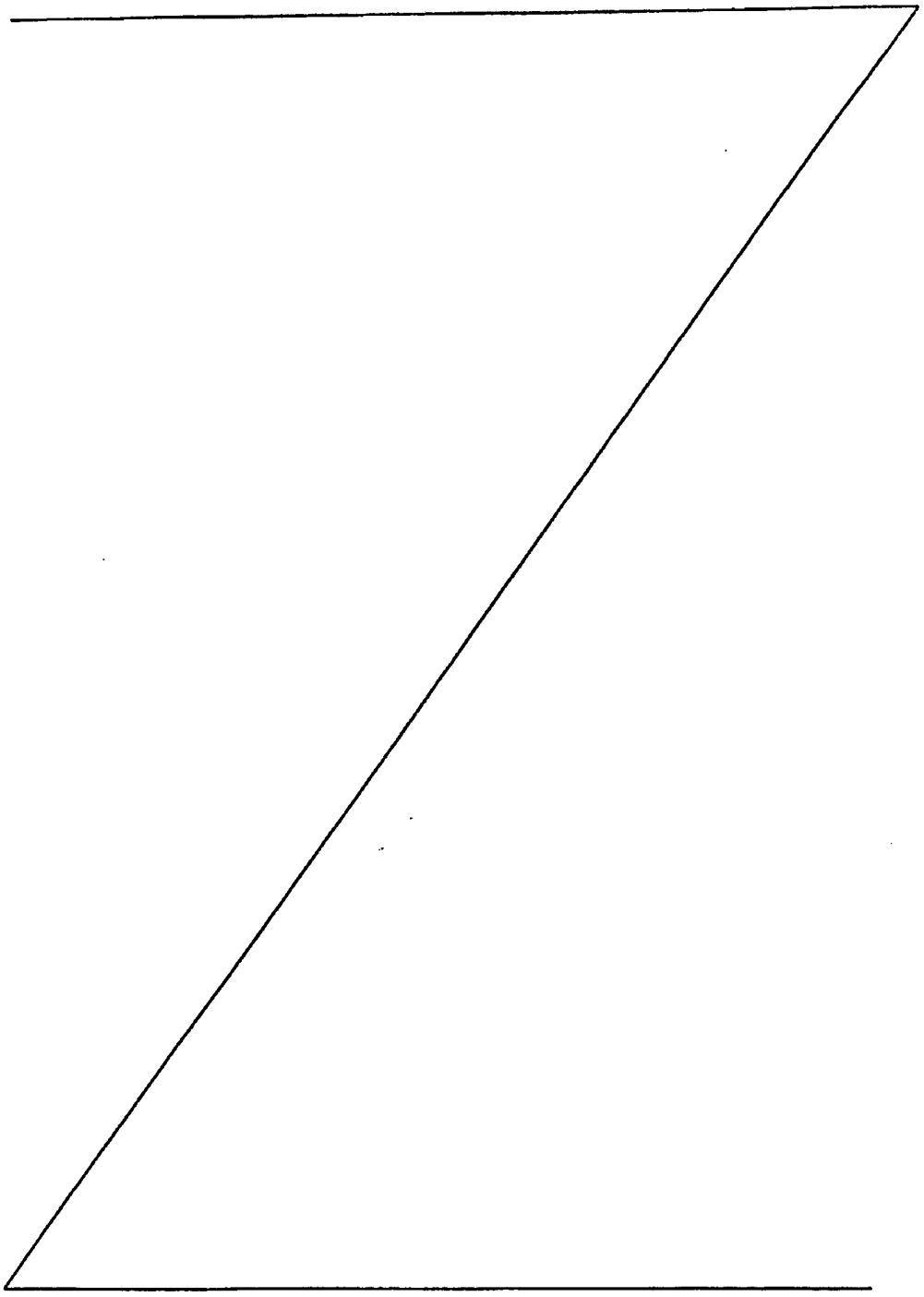
A is branched or unbranched $(C_{1-10})$-alkylene or straight-chain or branched $(C_{2-10})$-alkylene which comprises at least one group Z selected from the group consisting of O, S, $NR^2$, cyclopropyl, CHOH, a double and a triple bond,

$R^2$ is hydrogen or $C_1$-$C_4$-alkyl,

B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine or the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

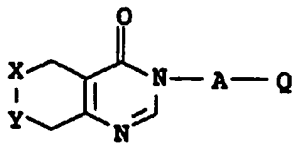
Ar is phenyl which is unsubstituted or substituted by $(C_{1-6})$-alkyl, branched or unbranched, O-$(C_{1-6})$-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, $NR^2_2$, $CO_2R^2$, cyano or phenyl, is tetralin, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or

substituted by $(C_{1-4})$-alkyl or O-$(C_{1-4})$-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from



the group consisting of O and N, and which may be fused with other aromatic radicals.

These compounds of the formula I can be prepared by reacting a compound of the formula II

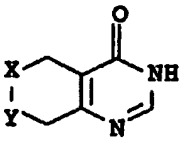


(II),

in which A, X and Y are as defined above and Q is a group that can be cleaved off (for example Cl, Br, I, alkanesulfonyloxy or arylsulfonyloxy), with a compound of the formula III

H-B-Ar (III),

in which B and Ar are as defined above, in a manner known per se and converting the resulting compound, if appropriate, into the acid addition salt of a physiologically acceptable acid. It is also possible to react a compound of the formula IV



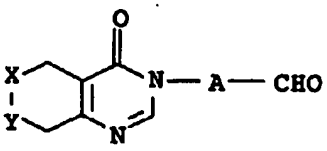
(IV)

with a compound of the formula V

Q-A-B-Ar (V)

in a manner known per se.

A further synthesis variant is the attachment of a compound of the formula VI



(VI)

to a compound of the formula III by a reductive amination, which is known per se.

The compounds of the formula III can be synthesized by

1. attaching compounds of the formula VII

$$W\text{-}B^1 \qquad (VII),$$

where $B^1$ is piperazine or homopiperazine and W is hydrogen or one of the customary amino protective groups (such as, for example, Boc or Cbz), to a compound of the formula VIII

$$P\text{-}Ar \qquad (VIII),$$

where P is $B(OH)_2$, $SnR_3$, OTf, Br, Cl or I and R is $C_1$-$C_4$-alkyl, in a manner known per se; or

2. attaching compounds of the formula IX

$$W\text{-}B^2\text{-}P^1 \qquad (IX),$$

where $B^2$ is 4-tetrahydro-1,2,3,6-pyridine or the corresponding cyclic compounds which are enlarged by a methylene group and $P^1$ is Cl, Br, I, $SnR_3$ - where R is $C_1$-$C_4$-alkyl - , OTf, to a compound of the formula X

$$P\text{-}Ar \qquad (X),$$

where W, P and Ar are each as defined above, and where the reactions are carried out by known processes, such as, for example, those described in

S.L. Buchwald et al. *J. Am. Chem. Soc.* **1996**, *118*, 7215,
J.F. Hartwig et al. *Tetrahedron Lett.* **1995**, *36*, 3604,
J.K. Stille et al. *Angew. Chem.* **1986**, *98*, 504,
S.L. Buchwald et al. *Angew. Chem.* **1995**, *107*, 1456 or
J.F. Hartwig et al. *J. Am. Chem. Soc* **1996**, *118*, 7217 or
J.F. Hartwig et al. *J. Org. Chem.* **1997**, *62*, 1268,
S.L. Buchwald et al. *J. Org. Chem.* **1997**, *62*, 1264 and literature cited therein or
S.L. Buchwald et al *J. Am. Chem. Soc* **1997**, *119*, 6054,
J.K. Stille, *Angew. Chem.* **1986**, *98*, 504 or
J.K. Stille et al. *J. Org. Chem.* **1990**, *55*, 3014,
M. Pereyre et al. "Tin in Organic Synthesis", Butterworth 1987; or

3. reducing compounds of the formula (XI)

$$W\text{-}B^2\text{-}Ar \qquad (XI),$$

where $B^2$ is as defined above, to give compounds of the formula XII

$$W\text{-}B^3\text{-}Ar \qquad (XII),$$

in which $B^3$ is a piperidine which is attached in 1,4 position or the corresponding cyclic compounds which are enlarged by a methylene group; or

4. cyclizing compounds of the formula XIII

$$W\text{-}N\text{-}(C_2H_4Q)_2 \qquad (XIII),$$

where W and Q are as defined above, with a compound of the formula XIV

$$NH_2\text{-}Ar \qquad (XIV),$$

where Ar is as defined above, to give compounds of the formula XV

$$W\text{-}B^1\text{-}Ar \qquad (XV).$$

The substances of the formulae III and V required as starting materials for synthesizing the novel compounds are known or can be prepared according to known processes (for example *Organikum* Barth Dt. Verl. der Wiss. 1993 or A. R. Katritzky, C. W. Rees (ed.) *Comprehensive Heterocyclic Chemistry* Pergamon Press) from analogous starting materials.

The further reaction of the compounds

$$H\text{-}B\text{-}Ar \qquad (III)$$

prepared in this manner according to 1. to 4. with subsequent removal of any protective groups to give the compounds of the formula V is carried out by attachment to compounds of the formula XVI

$$Q\text{-}A\text{-}Q' \qquad (XVI),$$

where Q and Q' are leaving groups, under conditions known per se.

The substances of the formulae II, IV, VI and of the formulae P-Ar, $NH_2$-Ar, W-$B^1$ or W-$B^2$-$P^1$ required as starting materials for synthesizing the novel compounds are known or can be prepared according to the preparation processes described in the literature from analogous starting materials (for example B. Dumaitre, N. Dodic *J. Med. Chem.* 1996, *39*, 1635 or A. Yokoo et al. *Bull. Chem. Soc. Jpn.* 1956, *29*, 631 or L. Börjeson et al. *Acta Chem. Chem.* 1991, *45*, 621 or *Organikum* Barth Dt. Verl. der Wiss. 1993 or A. R. Katritzky, C. W. Rees (ed.) *Comprehensive Heterocyclic Chemistry* Pergamon Press or *The Chemistry of Heterocyclic Compounds* J. Wiley & Sons Inc. NY and the literature cited therein in each case).

Example 1:

3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4(3H)-one

Preparation of the starting materials

a) 5,6,7,8-Tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4(3H)-one

4.7 g of sodium were, a little at a time, allowed to react in 250 ml of ethanol, and a suspension of 14.2 g (0.05 mol) of methyl N-benzyl-4-piperidone-3-carboxylate in ethanol was then added dropwise at 5-10°C. The mixture was stirred for 30 minutes, after which 6 g (0.075 mol) of formamidine hydrochloride were added slowly, and the reaction mixture was heated under reflux for 10 h. The solvent was removed under reduced pressure and the residue was taken up in 100 ml of water and adjusted to pH = 6.5 - 7 using 2N of hydrochloric acid, so that the product precipitated out. The crystals were filtered off with suction and dried in a vacuum drying cabinet, giving 8 g (66%). m.p.: 88°C.

5,6,7,8-Tetrahydro-7-benzylpyrido-[3,4-d]pyrimidin-4(3H)-one (m.p.: 199°C) and methyl 5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4(3H)-one-6-carboxylate (m.p.: 160°C) were obtained similarly.

b) 1-(2-Methoxyphenyl)-4-(2-chloroeth-1-yl)piperazine

At room temperature, a solution of 19.2 g (0.1 mol) of o-methoxyphenylpiperazine and 13.8 g (0.1 mol) of potassium carbonate in 200 ml of DMF was initially charged and, after

30 min, 30 ml (0.36 mol) of 1-bromo-2-chloroethane were added. The mixture was stirred at room temperature for 2 h. The mixture was poured into ice-water and then extracted with methyl tert-butyl ether, and the organic phases were washed with water, dried with sodium sulfate and subsequently concentrated. The residue was dissolved in ethyl acetate and the hydrochloride was precipitated out by addition of 30% strength isopropanol/HCl solution, filtered off with suction and then dried at 40°C in a vacuum drying cabinet. This gave 17 g (67%) of substance. m.p.: 200°C.

1-(2-Methoxyphenyl)-4-(3-chloroprop-1-yl)piperazine (m.p.: 217°C, hydrochloride), 1-(3,4-methylphenyl)-4-(2-chloroeth-1-yl)-piperazine (m.p.: 260°C, hydrochloride), 1-(2-pyrimidyl)-4-(2-chloroeth-1-yl)piperazine (m.p.: 270°C, hydrochloride), 1-(naphth-1-yl)-4-(3-chloroprop-1-yl)piperazine (m.p.: 217°C, hydrochloride), were obtained in a similar manner.

Two exemplary syntheses for preparing the piperazines are shown below.

1-Tetralin-5-yl-piperazine

14.7 g (0.1 mol) of 5-aminotetralin and 18 g (0.11 mol) of bis(β-chloroethyl)amine hydrochloride in 300 ml of n-butanol were refluxed for 48 h, 5.4 g of sodium carbonate were added after cooling and the mixture was once more refluxed for 20 h. The precipitate which was formed by cooling was filtered off with suction, taken up in water and admixed with 2N sodium hydroxide solution. The aqueous phase was extracted with ethyl acetate, and the extract was washed with water, dried over sodium sulfate and concentrated under reduced pressure. In this manner, it was possible to isolate 10.7 g (50%) of the product as an oil.

4-Piperazin-1-ylisoquinoline

4.51 g (21.7 mmol) of 4-bromoisoquinoline, 4.65 g (25.0 mmol) of t-butyl piperazine-N-carboxylate, 0.1 g (0.11 mmol) of tris-(dibenzylideneacetone)dipalladium, 0.11 g (0.18 mmol) of 2,2'-bis(diphenylphosphino)-1,1'-dinaphthyl and 2.92 g (30.4 mmol) of sodium t-butoxide were admixed in 50 ml of toluene and stirred at 75°C for 2 h. The reaction mixture was poured onto ice/sodium chloride and extracted with ethyl acetate, the organic phase was dried over sodium sulfate and the solvent was removed using a rotary evaporator. The product crystallized out, and it was filtered off with suction and washed with pentane. This gave

5.5 g (81%) of the Boc-protected piperazine (m.p.: 111°C). 5.2 g (16.6 mmol) of this substance were taken up in 17 ml of dichloromethane and, at 0°C, slowly admixed with 17 ml (0.22 mol) of trifluoroacetic acid. The mixture was stirred at 0°C for 4 h, poured onto ice-water and extracted with dichloromethane. The aqueous phase was filtered, made alkaline and extracted with dichloromethane. After drying over sodium sulfate and substantial removal of the solvent, the residue was diluted with diethyl ether and the hydrochloride was precipitated out using ethereal hydrochloric acid. This gave 3.2 g (67%) of the product. (m.p.: 293°C).

The following compounds were prepared similarly to the two processes described: 1-naphth-1-ylazepane (85°C, hydrochloride), 1-naphth-1-ylmethylpiperazine (oil), 4-piperazin-1-yl-indane (oil), 1-naphth-1-ylpiperazine (82°C), 4-chloro-1-piperazin-1-ylphthalazine (205°C, decomp.) and 4-piperazin-1-ylquinazoline (320°C, hydrochloride). Other derivatives were commercially available.

Preparation of the end product

2.9 g (10 mmol) of chloroethylpiperazine [b)] and 2.8 g (20 mmol) of potassium carbonate were added to a solution of 2.4 g (10 mmol) of tetrahydropyridopyrimidine [a)] in 40 ml of DMF. The reaction mixture was reacted at 90°C for two hours and then poured onto ice-water and extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution and dried over sodium sulfate, and the solvent was removed under reduced pressure. The oil that remained was taken up in acetone, and the hydrochloride was precipitated out using isopropanol/HCl. This gave 4 g (75%) of the product (m.p.: 205°C).

NMR: $CDCl_3$ $\delta$ 8.0 (s, 1H), 7.4 - 7.2 (m, 5H), 7.1 - 6.8 (m, 4H), 4.0 (t, 2H), 3.8 (s, 3H), 3.7 (s, 2H), 3.5 (s, 2H), 3.1 (brd. s, 4H), 2.8 - 2.6 (m, 10H) ppm.

The following compounds were obtained in a similar manner:

Example 2:

3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-benzylpyrido[3,4-d]pyrimidin-4(3H)-one (m.p.: 181°C, hydrochloride).

Example 3:

3-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4(3H)-one (m.p.: 198°C, hydrochloride).

Example 4:

3-[3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-5,6,7,8-tetrahydro-7-benzylpyrido[3,4-d]pyrimidin-4(3H)-one (m.p.: 190°C, hydrochloride).

Example 5:

3-[3-[4-(2-methoxyphenyl)-1-piperazinyl]2-hydroxypropyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one.

Example 6:

t-butyl 3-[2-[4-(naphth-1-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-(3H)-one-6-carboxylate (m.p.: 170°C, hydrochloride).

Example 7:

3-[2-[4-(isoquinolin-4-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 268°C, hydrochloride).

Example 8:

3-[2-[4-(naphth-1-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydropyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 272°C, hydrochloride).

Example 9:

3-[2-[4-(quinazolin-4-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 258°C, hydrochloride).

Example 10:

3-[2-[4-(naphth-1-yl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 227°C, hydrochloride).

Example 11:

3-[2-[4-(naphth-1-yl)-tetrahydro-1,2,3,6-pyridin-1-yl]eth-1-yl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one (m.p.: 216°C, hydrochloride).

Synthesis of the starting materials

a) N-Boc-4-(trifluoromethanesulfonyloxy)-tetrahydro-1,2,3,6-pyridine

At -78°C, a solution of 13.2 g (0.13 mol) of diisopropylamine in 200 ml of THF was deprotonated using 100 ml of nBuLi (1.6M in hexane), and, after 30 minutes at this temperature, 20.0 g (0.1 mol) of N-Boc-piperid-4-one dissolved in 50 ml of THF were added dropwise. After a further three hours at -78°C, a solution of 39.3 g (0.11 mol) of N,N-bistrifluoromethanesulfonylaniline in 50 ml of THF was added, and the mixture was allowed to warm to room temperature overnight. For work-up, the mixture was admixed with water and extracted with ether, the organic phases were washed with $NaHCO_3$ solution and water and dried over sodium sulfate, and the solvent was concentrated. The crude product was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 3/1).

Yield: 20.2 g (60% of theory)

1H NMR:(270 MHz,$CDCl_3$) δ = 1.4 (s, 9H); 2.4 (m, 2H); 3.6 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H) ppm

b) N-Boc-4-naphth-1-yltetrahydro-1,2,3,6-pyridine

22 ml of 2M sodium carbonate solution, 7.63 g (44.4 mmol) of naphthyl-1-boronic acid, 4.13 g (97.6 mmol) of lithium chloride, 0.85 g (4.44 mmol) of copper(I) iodide and 2.1 g (1.77 mmol) of tetrakistriphenylpalladium were added successively to 14.7 g (44.4 mmol) of the compound described above dissolved in 115 ml of dimethoxyethane, and the mixture was heated at the boil for 4 h. For work-up, aqueous ammonia solution was added and the mixture was extracted with water and ethyl acetate, the extract was dried over sodium sulfate and the residue which was obtained after evaporation of the solvent was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 4/1).

Yield: 8.2 g (57% of theory)

1H-NMR (270 MHz, $CDCl_3$): δ = 1.4 (s, 9H); 2.5 (m, 2H); 3.7 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H); 7.2-7.5(m, 3H); 7.3-8.0 (m, 3H) ppm.

c) 4-Naphth-1-yltetrahydro-1,2,3,6-pyridine

7.84 g (25.3 mmol) of N-Boc-4-naphth-1-yltetrahydro-1,2,3,6-pyridine were stirred overnight at room temperature with 200 ml of ethereal hydrochloric acid, and the precipitated product was filtered off and dried.

Yield: 5.5 g (88% of theory).

d) Preparation of the end product

0.51 g (2 mmol) of 4-naphth-1-yltetrahydro-1,2,3,6-pyridine dissolved in 30 ml of dry DMF was admixed with 0.61 g (2 mmol) of 3-(2-chloroeth-1-yl)-3,5,7,8-tetrahydro-4-oxo-6-benzylpyrido[4,3-d]pyrimidine and with 2 ml (17 mmol) of triethylamine, and the mixture was stirred at 120°C for 5 h. The organic phase was diluted with ether, washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure. The resulting crude product was purified chromatographically, giving a white solid by precipitating the salt using ethereal hydrochloric acid solution.

Yield: 0.2 g (20% of theory)

m.p.: 237°C.

Example 12

3-[2-[4-(Naphth-1-yl)piperidin-1-yl]eth-1-yl]-5,6,7,8-tetrahydro-6-benzylpyrido[4,3-d]pyrimidin-4-(3H)-one

4-Naphth-1-ylpiperidine

3.7 g (15.3 mmol) of 4-naphth-1-yltetrahydro-1,2,3,6-pyridine, dissolved in methanol, were hydrogenated at room temperature with hydrogen for 48 h, with addition of 0.8 g of palladium on carbon. The catalyst was filtered off and the solvent was concentrated.

Yield: 1.8 g (56% of theory)

1H NMR (270 MHz, $CDCl_3$) δ = 1.6-1.8 (m, 2H); 2.0 (m, 2H); 2.9 (dt, 2H); 3.3 (d, 2H); 3.5 (tt, 1H); 7.4-7.6 (m, 4H); 7.7 (d, 1H); 7.9 (d, 1H); 8.1 (d, 1H) ppm.

Preparation of the end product

0.42 g (2 mmol) of 4-naphth-1-ylpiperidine, dissolved in 30 ml of dry DMF, was admixed with 0.61 g (2 mmol) of 3-(2-chloroeth-1-yl)-3,5,7,8-tetrahydro-4-oxo-6-benzylpyrido[4,3-d]pyrimidine and with 2 ml (17 mmol) of triethylamine, and the mixture was stirred at 120°C for 5 h. The organic phase was diluted with ether, washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure. The resulting crude product was purified chromatographically, giving a white solid by precipitating the salt using ethereal hydrochloric acid solution.

Yield: 0.24 g (27% of theory)

1H NMR (270 MHz, $CDCl_3$) δ = 8.3 (s, 1H), 8.0 (d, 1H), 7.8 (d, 1H), 7.7 (t, 1H), 7.5 - 7.2 (m, 9H), 4.5 (s, 2H), 4.0 (s, 2H), 3.7 - 2.3 (m, 15H), 2.1 (d, 2H) ppm.

Other preferred compounds of the formula I according to the invention are listed in the table below.

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 13. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | 235°C |
| 14. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | 236°C |
| 15. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | 245°C |
| 16. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 4-quinazoline | 270°C |
| 17. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-quinazoline | 260°C |
| 18. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 4-isoquinoline | 286°C |
| 19. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-isoquinoline | 290°C |
| 20. | $NR^1$ | $CH_2$ | Ph-$CH_2$ | $C_4$ | | 4-piperazine-1-yl | 2-pyrimidine | 265°C |
| 21. | $NR^1$ | $CH_2$ | Ph-$CH_2$ | $C_3$ | | 4-piperazine-1-yl | 4-indane | 281°C |
| 22. | $NR^1$ | $CH_2$ | Ph-$CH_2$ | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | 225°C |
| 23. | $NR^1$ | $CH_2$ | Ph-$CH_2$ | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | 250°C |
| 24. | $NR^1$ | $CH_2$ | Ph-$CH_2$ | $C_2$ | | 4-piperazine-1-yl | 6-$CF_3$-2-pyrimidine | 145°C (free base) |
| 25. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_3$ | | 4-piperazine-1-yl | 3-$CF_3$-Ph | 217°C |
| 26. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperazine-1-yl | 6-$CH_3$-2-pyridine | 132°C |
| 27. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperazine-1-yl | 4-$CF_3$-2-pyridine | 130°C |
| 28. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperazine-1-yl | 3-$CF_3$-Ph | 158°C |
| 29. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-$CF_3$-Ph | 196°C |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 30. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | 235°C |
| 31. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-$CF_3$-2-pyridine | 253°C |
| 32. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-$CF_3$-Ph | 168°C |
| 33. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 34. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OH-Ph | |
| 35. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 36. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |
| 37. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-CN-Ph | |
| 38. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | |
| 39. | $NR^1$ | $CH_2$ | H | $C_2$ | Me | 4-piperazine-1-yl | 3-$NR^2_2$-Ph | |
| 40. | $NR^1$ | $CH_2$ | H | $C_2$ | Me | 4-piperazine-1-yl | 3-$CO_2R^2$-Ph | |
| 41. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-$NO_2$-Ph | |
| 42. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-F-Ph | |
| 43. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-$iC_3$-Ph | |
| 44. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-I-Ph | |
| 45. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-Br-Ph | |
| 46. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-O(n-$C_4$)-Ph | |
| 47. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-t-Bn-Ph | |
| 48. | $NR^1$ | $CH_2$ | H | $C_2$ | H | 4-piperazine-1-yl | 4-$CO_2R^2$-Ph | |
| 49. | $NR^1$ | $CH_2$ | H | $C_2$ | n-$C_3$ | 4-piperazine-1-yl | 4-$NR^2_2$-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 50. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-Me,4-Me-Ph | |
| 51. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Cl,4-$NO_2$-Ph | |
| 52. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-tBu,5-$CF_3$-Ph | |
| 53. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OMe,5-Ph-Ph | |
| 54. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OMe,4-Cl,5-Me-Ph | |
| 55. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |
| 56. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 57. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OMe-1-naphthalene | |
| 58. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 59. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 8-OMe-1-naphthalene | |
| 60. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-Indol | |
| 61. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-quinazoline | |
| 62. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-quinoxaline | |
| 63. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 1-phthalazine | |
| 64. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 65. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 1-isoquinoline | |
| 66. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 67. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-tBu,4-$CF_3$-6-pyrimidine | |
| 68. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 69. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Ph-4-quinazoline | |
| 70. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 5-chromane | |
| 71. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 3-isoxazole | |
| 72. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 7-OMe-1-naphthalene | |
| 73. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 1-tetraline | |
| 74. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Et-naphthalene | |
| 75. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperazine-1-yl | 2-quinoline | |
| 76. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 77. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-OH-Ph | |
| 78. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |
| 79. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-CN-Ph | |
| 80. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | Me | 4-piperazine-1-yl | 3-$NR^2_2$-Ph | |
| 81. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | Me | 4-piperazine-1-yl | 3-$CO_2R^2$-Ph | |
| 82. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-$CF_3$-Ph | |
| 83. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-$NO_2$-Ph | |
| 84. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-F-Ph | |
| 85. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-$iC_3$-Ph | |
| 86. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-I-Ph | |
| 87. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-Br-Ph | |
| 88. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-O(n-$C_4$)-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 89. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-tBu-Ph | |
| 90. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | H | 4-piperazine-1-yl | 4-$CO_2R^2$-Ph | |
| 91. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | n-$C_3$ | 4-piperazine-1-yl | 4-$NR^2_2$-Ph | |
| 92. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-Me,4-Me-Ph | |
| 93. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Cl,4-$NO_2$-Ph | |
| 94. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-tBu,5-$CF_3$-Ph | |
| 95. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-OMe,5-Ph-Ph | |
| 96. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-OMe,4-Cl,5-MePh | |
| 97. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 98. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-OMe-1-naphthalene | |
| 99. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 100. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 8-OMe-1-Naphtalin | |
| 101. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-Indol | |
| 102. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-quinazoline | |
| 103. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-quinoxaline | |
| 104. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 1-phthalazine | |
| 105. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 106. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 1-isoquinoline | |
| 107. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 7-benzofuran | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 108. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-tBu,4-$CF_3$-6-pyrimidine | |
| 109. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |
| 110. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Ph-4-quinazoline | |
| 111. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 5-chromane | |
| 112. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-isoxazole | |
| 113. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 7-OMe-1-naphthalene | |
| 114. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 1-tetraline | |
| 115. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Et-naphthalene | |
| 116. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-quinoline | |
| 117. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 118. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-OH-Ph | |
| 119. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 120. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |
| 121. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-CN-Ph | |
| 122. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | |
| 123. | $NR^1$ | $CH_2$ | Me | $C_2$ | Me | 4-piperazine-1-yl | 3-$NR^2_2$-Ph | |
| 124. | $NR^1$ | $CH_2$ | Me | $C_2$ | Me | 4-piperazine-1-yl | 3-$CO_2R^2$-Ph | |
| 125. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-$NO_2$-Ph | |
| 126. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-F-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 127. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-$iC_3$-Ph | |
| 128. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-I-Ph | |
| 129. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-Br-Ph | |
| 130. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-O(n-$C_4$)-Ph | |
| 131. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-tBu-Ph | |
| 132. | $NR^1$ | $CH_2$ | Me | $C_2$ | H | 4-piperazine-1-yl | 4-$CO_2R^2$-Ph | |
| 133. | $NR^1$ | $CH_2$ | Me | $C_2$ | n-$C_3$ | 4-piperazine-1-yl | 4-$NR^2_2$-Ph | |
| 134. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-Me,4-Me-Ph | |
| 135. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Cl,4-$NO_2$-Ph | |
| 136. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-tBn,5-$CF_3$-Ph | |
| 137. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-OMe,5-Ph-Ph | |
| 138. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-OMe,4-Cl,5-MePh | |
| 139. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |
| 140. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 141. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-OMe-1-naphthalene | |
| 142. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 143. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 8-OMe-1-naphthalene | |
| 144. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-Indol | |
| 145. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-quinazoline | |
| 146. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-quinazoline | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 147. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-quinoxaline | |
| 148. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 1-phthalazine | |
| 149. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 150. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 1-isoquinoline | |
| 151. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 152. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 7-benzofuran | |
| 153. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 154. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-tBu,4-$CF_3$-6-pyrimidine | |
| 155. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |
| 156. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Ph-4-quinazoline | |
| 157. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 5-chromane | |
| 158. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 3-isoxazole | |
| 159. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 7-OMe-1-naphthalene | |
| 160. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 1-tetraline | |
| 161. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Et-naphthalene | |
| 162. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-quinoline | |
| 163. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 164. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 165. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 166. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | |
| 167. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 3-CN-Ph | |
| 168. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 4-F-Ph | |
| 169. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |
| 170. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 171. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-Me-naphthalene | |
| 172. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 8-OMe-naphthalene | |
| 173. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-quinazoline | |
| 174. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 1-phthalazine | |
| 175. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 176. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 177. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-tBu,4-$CF_3$-6-pyrimidine | |
| 178. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |
| 179. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 180. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 181. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |
| 182. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | |
| 183. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 3-CN-Ph | |
| 184. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 3-tBu,5-$CF_3$-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 185. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |
| 186. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 187. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 188. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 189. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 8-OMe-1-naphthalene | |
| 190. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 4-quinazoline | |
| 191. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 192. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 193. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 194. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-tBu,4-$CF_3$-6-pyrimidine | |
| 195. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |
| 196. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 197. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 198. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |
| 199. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | |
| 200. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 3-CN-Ph | |
| 201. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 4-F-Ph | |
| 202. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 3-tBu, 5-$CF_3$-Ph | |
| 203. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 204. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 205. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-OMe-1-naphthalene | |
| 206. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 207. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 8-OMe-1-naphthalene | |
| 208. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 4-quinazoline | |
| 209. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-quinazoline | |
| 210. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 1-phthalazine | |
| 211. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 212. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 213. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 214. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-tBu,4-$CF_3$-pyrimidine | |
| 215. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |
| 216. | $NR^1$ | $CH_2$ | i-$C_3$ | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 217. | $NR^1$ | $CH_2$ | $C_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 218. | $NR^1$ | $CH_2$ | $C_2$-(2-OMe)-Ph | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 219. | $NR^1$ | $CH_2$ | $C_3$-(4-Cl)Ph | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 220. | $NR^1$ | $CH_2$ | $C_2$-(2-$CF_3$)-Ph | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 221. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-piperazine-1-yl | 5-tetraline | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 222. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 223. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 224. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 225. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 226. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 227. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_3$ | | 4-piperazine-1-yl | 5-tetraline | |
| 228. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 229. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_3$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 230. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_3$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 231. | $NR^1$ | $CH_2$ | Me | $C_3$ | | 4-piperazine-1-yl | 5-tetraline | |
| 232. | $NR^1$ | $CH_2$ | Me | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 233. | $NR^1$ | $CH_2$ | Me | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 234. | $NR^1$ | $CH_2$ | Me | $C_3$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 235. | $NR^1$ | $CH_2$ | Me | $C_3$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 236. | $NR^1$ | $CH_2$ | Me | $C_3$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 237. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-piperazine-1-yl | 5-tetraline | |
| 238. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-piperazine-1-yl | 1-Napthalin | |
| 239. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 240. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 241. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-piperazine-1-yl | 2-pyrimidine | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 242. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 243. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_3$ | | 4-piperazine-1-yl | 5-tetraline | |
| 244. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 245. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 246. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_3$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 247. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_3$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 248. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 249. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 5-tetraline | |
| 250. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 1-Napthalin | |
| 251. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 252. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 253. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 254. | $NR^1$ | $CH_2$ | Ph-C=O | $C_3$ | | 4-piperazine-1-yl | 2-OMe-naphthalene | |
| 255. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 256. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 257. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 258. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 259. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 260. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-piperidine-1-yl | 2-OMe-naphthalene | |
| 261. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 262. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 263. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 264. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 265. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 266. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-piperidine-1-yl | 2-OMe-naphthalene | |
| 267. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 268. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 269. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 270. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 271. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 2-OMe-naphthalene | |
| 272. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 273. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 274. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 275. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 276. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 277. | $NR^1$ | $CH_2$ | $CH_3C$=O | $C_2$ | | 4-piperidine-1-yl | 2-OMe-naphthalene | |
| 278. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 279. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 280. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 281. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 282. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 283. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-piperidine-1-yl | 2-OMe-naphthalene | |
| 284. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 285. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 286. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 287. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 288. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 289. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 2-OMe-naphthalene | |
| 290. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 5-tetraline | |
| 291. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 292. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 293. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 294. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 295. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 296. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 5-tetraline | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 297. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 298. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 299. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 300. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 301. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 302. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | tetraline | |
| 303. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 304. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 305. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 306. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 307. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | tetraline | |
| 308. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 309. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 310. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 311. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 312. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 313. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | tetraline | |
| 314. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 315. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 316. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 317. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 318. | $NR^1$ | $CH_2$ | $CH_3C=O$ | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 319. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | tetraline | |
| 320. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |



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| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 321. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 322. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 323. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 324. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 325. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 326. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-homopiperazine-1-yl | 2-OMe-Ph | |
| 327. | $NR^1$ | $CH_2$ | H | $C_2$ | | 4-homopiperazine-1-yl | 2-OMe-1-naphthalene | |
| 328. | $NR^1$ | $CH_2$ | H | $C_3$ | | 4-homopiperazine-1-yl | 2-pyrimidine | |
| 329. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 330. | $NR^1$ | $CH_2$ | Me | $C_2$ | | 4-homopiperazine-1-yl | 2-OMe-Ph | |
| 331. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 332. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_3$ | | 4-homopiperazine-1-yl | 2-OMe-Ph | |
| 333. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 334. | $NR^1$ | $CH_2$ | Boc | $C_2$ | | 4-homopiperazine-1-yl | 2-OMe-Ph | |
| 335. | $NR^1$ | $CH_2$ | Boc | $C_3$ | | 4-homopiperazine-1-yl | 2-OMe-1-naphthalene | |
| 336. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 337. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_2$ | | 4-homopiperazine-1-yl | 2-OMe-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 338. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 339. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-homopiperazine-1-yl | 1-OMe-Ph | |
| 340. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$ | | 4-homopiperazine-1-yl | 2-pyrimidine | |
| 341. | $NR^1$ | $CH_2$ | H | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 342. | $NR^1$ | $CH_2$ | H | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 343. | $NR^1$ | $CH_2$ | H | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 344. | $NR^1$ | $CH_2$ | Me | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 345. | $NR^1$ | $CH_2$ | Me | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 346. | $NR^1$ | $CH_2$ | Me | $CH_2$-C($CH_2$)-$CH_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 347. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 348. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 349. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-C($CH_2$)-$CH_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 350. | $NR^1$ | $CH_2$ | Boc | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 351. | $NR^1$ | $CH_2$ | Boc | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 352. | $NR^1$ | $CH_2$ | Boc | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 353. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 354. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 355. | $NR^1$ | $CH_2$ | Ph-C=O | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 356. | $NR^1$ | $CH_2$ | Ph-C=O | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 357. | $NR^1$ | $CH_2$ | H | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 358. | $NR^1$ | $CH_2$ | H | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 359. | $NR^1$ | $CH_2$ | H | $CH_2$-C(OH)-$CH_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 360. | $NR^1$ | $CH_2$ | Me | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 361. | $NR^1$ | $CH_2$ | H | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 362. | $NR^1$ | $CH_2$ | H | $CH_2$-C(OH)-$CH_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 363. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 364. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-C(OH)-$CH_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 365. | $NR^1$ | $CH_2$ | Boc | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 366. | $NR^1$ | $CH_2$ | Boc | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 367. | $NR^1$ | $CH_2$ | Boc | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 368. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 369. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 370. | $NR^1$ | $CH_2$ | Ph-C=O | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 371. | $NR^1$ | $CH_2$ | Ph-C=O | $CH_2$-C(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 372. | $NR^1$ | $CH_2$ | H | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 373. | $NR^1$ | $CH_2$ | H | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 374. | $NR^1$ | $CH_2$ | H | $C_2$-N(Me)-$C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 375. | $NR^1$ | $CH_2$ | Me | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 376. | $NR^1$ | $CH_2$ | Me | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 377. | $NR^1$ | $CH_2$ | Me | $C_2$-N(Me)-$C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 378. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 379. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 380. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $C_2$-N(Me)-$C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 381. | $NR^1$ | $CH_2$ | Boc | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 382. | $NR^1$ | $CH_2$ | Boc | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 383. | $NR^1$ | $CH_2$ | Boc | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 384. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 385. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 386. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 387. | $NR^1$ | $CH_2$ | Ph-C=O | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 388. | $NR^1$ | $CH_2$ | H | $CH_2$-$CH(CH_3)$-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 389. | $NR^1$ | $CH_2$ | H | $CH_2$-$CH(CH_3)$-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 390. | $NR^1$ | $CH_2$ | H | $CH_2$-$CH(CH_3)$-$CH_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 391. | $NR^1$ | $CH_2$ | Me | $CH_2$-$CH(CH_3)$-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 392. | $NR^1$ | $CH_2$ | Me | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 393. | $NR^1$ | $CH_2$ | Me | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 394. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 395. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 396. | $NR^1$ | $CH_2$ | $CH_2$-Ph | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 397. | $NR^1$ | $CH_2$ | Boc | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 398. | $NR^1$ | $CH_2$ | Boc | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 399. | $NR^1$ | $CH_2$ | Boc | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 400. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 401. | $NR^1$ | $CH_2$ | $CH_3$-C=O | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 402. | $NR^1$ | $CH_2$ | Ph-C=O | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 403. | $NR^1$ | $CH_2$ | Ph-C=O | $CH_2$-CH($CH_3$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 404. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | Ph | |
| 405. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Me-Ph | |
| 406. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-CN-Ph | |
| 407. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Cl-Ph | |
| 408. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-$CF_3$-Ph | |
| 409. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-$iC_3$-Ph | |
| 410. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 3-Me, 4-Me-Ph | |
| 411. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |
| 412. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-indane | |
| 413. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 414. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-OMe-1-naphthalene | |
| 415. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 416. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 8-OMe-1-naphthalene | |
| 417. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-quinazoline | |
| 418. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 1-phthalazine | |
| 419. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-quinoline | |
| 420. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 4-isoquinoline | |
| 421. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 422. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperazine-1-yl | 2-pyridine | |
| 423. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 424. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 2-F-Ph | |
| 425. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 3-tBu-Ph | |
| 426. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 5-tetraline | |
| 427. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 428. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 2-OMe-1-naphthalene | |
| 429. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 430. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 1-isoquinoline | |
| 431. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperazine-1-yl | 2-Ph-4-quinazoline | |
| 432. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 433. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 434. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-Me-1-naphthalene | |
| 435. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-piperazine-1-yl | 2-pyrimidine | |
| 436. | $CH_2$ | $NR^1$ | $CH_3C{=}O$ | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 437. | $CH_2$ | $NR^1$ | $CH_3C{=}O$ | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 438. | $CH_2$ | $NR^1$ | $PhC{=}O$ | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 439. | $CH_2$ | $NR^1$ | $PhC{=}O$ | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 440. | $CH_2$ | $NR^1$ | Boc | $C_2$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 441. | $CH_2$ | $NR^1$ | Boc | $C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 442. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 443. | $CH_2$ | $NR^1$ | H | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |

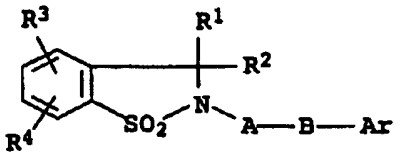
| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 444. | $CH_2$ | $NR^1$ | H | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 445. | $CH_2$ | $NR^1$ | Me | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 446. | $CH_2$ | $NR^1$ | Me | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 447. | $CH_2$ | $NR^1$ | Boc | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 448. | $CH_2$ | $NR^1$ | Boc | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 449. | $CH_2$ | $NR^1$ | $CH_3C=O$ | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 450. | $CH_2$ | $NR^1$ | $CH_3C=O$ | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 451. | $CH_2$ | $NR^1$ | PhC=O | $C_3$ | | 4-piperazine-1-yl | 2-OMe-Ph | |
| 452. | $CH_2$ | $NR^1$ | PhC=O | $C_3$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 453. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 454. | $CH_2$ | $NR^1$ | H | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 455. | $CH_2$ | $NR^1$ | Me | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 456. | $CH_2$ | $NR^1$ | Boc | $C_2$-N(Me)-$C_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 457. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 458. | $CH_2$ | $NR^1$ | H | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 459. | $CH_2$ | $NR^1$ | Me | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 460. | $CH_2$ | $NR^1$ | Boc | $CH_2$-C($CH_2$)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 461. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $CH_2$-CH(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 462. | $CH_2$ | $NR^1$ | H | $CH_2$-CH(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 463. | $CH_2$ | $NR^1$ | Me | $CH_2$-CH(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 464. | $CH_2$ | $NR^1$ | Boc | $CH_2$-CH(OH)-$CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 465. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $CH_2$-$CH(CH_3)CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 466. | $CH_2$ | $NR^1$ | H | $CH_2$-$CH(CH_3)CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 467. | $CH_2$ | $NR^1$ | Me | $CH_2$-$CH(CH_3)CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 468. | $CH_2$ | $NR^1$ | Boc | $CH_2$-$CH(CH_3)CH_2$ | | 4-piperazine-1-yl | 1-naphthalene | |
| 469. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 470. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 471. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 472. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 473. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 474. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Napthalin | |
| 475. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperidine-1-yl | 5-tetraline | |
| 476. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 477. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 478. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperidine-1-yl | 4-isoquinoline | |
| 479. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperidine-1-yl | 2-pyrimidine | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 480. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Napthalin | |
| 481. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 482. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 483. | $CH_2$ | $NR^1$ | Me | $C_3$ | | 4-piperidine-1-yl | 2-pyrimidine | |
| 484. | $CH_2$ | $NR^1$ | $CH_3$-C=O | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 485. | $CH_2$ | $NR^1$ | $CH_3$-C=O | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 486. | $CH_2$ | $NR^1$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 2-OMe-Ph | |
| 487. | $CH_2$ | $NR^1$ | Ph-C=O | $C_2$ | | 4-piperidine-1-yl | 1-naphthalene | |
| 488. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 5-tetraline | |
| 489. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 490. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-Ph | |
| 491. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 4-isoquinoline | |
| 492. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-pyrimidine | |
| 493. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 2-OMe-naphthalene | |
| 494. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |

| No. | X | Y | $R^1$ | A | $R^2$ | B | Ar | m.p. hydro-chloride |
|---|---|---|---|---|---|---|---|---|
| 495. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 496. | $CH_2$ | $NR^1$ | Boc | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 497. | $CH_2$ | $NR^1$ | $CH_3$-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 498. | $CH_2$ | $NR^1$ | Ph-C=O | $C_2$ | | 4-tetrahydro-1,2,3,6-pyridine-1-yl | 1-naphthalene | |
| 499. | $CH_2$ | $NR^1$ | $CH_2$-Ph | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 500. | $CH_2$ | $NR^1$ | H | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 501. | $CH_2$ | $NR^1$ | Me | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |
| 502. | $CH_2$ | $NR^1$ | Boc | $C_2$ | | 4-homopiperazine-1-yl | 1-naphthalene | |

DE 19746612.5 describes 2-substituted 1,2-benzisothiazole derivatives of the formula I



I

in which

$R^1$, $R^2$ independently of one another are $(C_{1-6})$-alkyl,

$R^3$, $R^4$ independently of one another are hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, OH, O-$(C_{1-6})$-alkyl, branched or unbranched, F, Cl, Br, I, trifluoromethyl, $NR^5R^6$, $CO_2R^7$, nitro, cyano, pyrrole, are a phenyl-$C_1$-$C_4$-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

$R^5$, $R^6$ independently of one another are hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, COPh, $CO_2tBu$, CO-$(C_{1-4})$-alkyl or together are a 5- or 6-membered ring which may contain a second nitrogen (for example piperazine),

$R^7$ is hydrogen or $(C_{1-6})$-alkyl, branched or unbranched,

A is branched or unbranched $(C_{1-10})$-alkylene or straight-chain or branched $(C_{2-10})$-alkylene which comprises at least one group Z selected from the group consisting of O, S, $NR^7$, cyclopropyl, CHOH, a double and a triple bond,

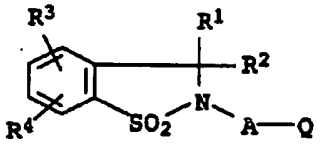
B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine and the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by $(C_{1-6})$-alkyl, branched or unbranched, O-$(C_{1-6})$-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, $NR^5R^6$, $CO_2R^7$, cyano or phenyl, is tetraline, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by $(C_{1-4})$-alkyl or O$(C_{1-4})$-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from the group consisting of O and N, and which may be fused with other aromatic radicals, for example

quinoline, isoquinoline, phthalazine, indole and quinazoline, which for its part may be substituted again by phenyl,

and their salts with physiologically acceptable acids.

These compounds of the formula I can be prepared by reacting a compound of the formula II

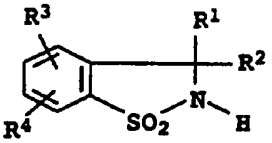


II,

in which $R^1$ to $R^4$ and A are as defined above and Q is a group that can be cleaved off (for example Cl, Br, I, alkanesulfonyloxy or arylsulfonyloxy), with a secondary amine of the formula III

H-B-Ar III,

in which B and Ar are as defined above, in a manner known per se and converting the resulting compound, if appropriate, into the acid addition salt of a physiologically acceptable acid. It is also possible to react a compound of the formula IV

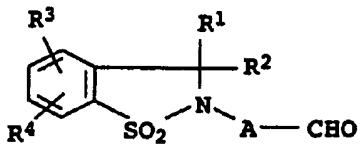


IV

with a compound of the formula V

Q-A-B-Ar V

in a manner known per se. A further synthesis variant is the attachment of a compound of the formula VI



VI

to a compound of the formula III by a reductive amination known per se.

The compounds of the formula III can be synthesized by

5. attaching compounds of the formula VII

$$W\text{-}B^1 \qquad (VII),$$

where $B^1$ is piperazine or homopiperazine and W is hydrogen or one of the customary amino protective groups (such as, for example, Boc or Cbz), to a compound of the formula VIII

$$P\text{-}Ar \qquad (VIII),$$

where P is $B(OH)_2$, $SnR_3$, OTf, Br, Cl or I and R is $C_1$-$C_4$-alkyl, in a manner known per se; or

6. attaching compounds of the formula IX

$$W\text{-}B^2\text{-}P^1 \qquad (IX),$$

where $B^2$ is 4-tetrahydro-1,2,3,6-pyridine or the corresponding cyclic compounds which are enlarged by a methylene group and $P^1$ is Cl, Br, I, $SnR_3$ - where R is $C_1$-$C_4$-alkyl - , OTf, to a compound of the formula X

$$P\text{-}Ar \qquad (X),$$

where W, P and Ar are each as defined above, and where the reactions are carried out by known processes, such as, for example, those described in
S.L. Buchwald et al. J. Am. Chem. Soc. 1996, 118, 7215
J.F. Hartwig et al. Tetrahedron Lett. 1995, 36, 3604
J.K. Stille et al. Angew. Chem. 1986, 98, 504
S.L. Buchwald et al. Angew. Chem. 1995, 107, 1456 or
J.F. Hartwig et al. J. Am. Chem. Soc 1996, 118, 7217 or
J.F. Hartwig et al. J. Org. Chem. 1997, 62, 1268
S.L. Buchwald et al. J. Org. Chem. 1997, 62, 1264 and literature cited therein or
S.L. Buchwald et al. J. Am. Chem. Soc 1997, 119, 6054
J.K. Stille, Angew. Chem. 1986, 98, 504 or
J.K. Stille et al. J. Org. Chem. 1990, 55, 3014.
M. Pereyre et al. "Tin in Organic Synthesis", Butterworth 1987; or

7. reducing compounds of the formula (XI)

$$W\text{-}B^2\text{-}Ar \qquad (XI),$$

where $B^2$ is as defined above, to give compounds of the formula XII

$$W\text{-}B^3\text{-}Ar \qquad (XII),$$

in which $B^3$ is a piperidine which is attached in 1,4-position or the corresponding cyclic compounds which are enlarged by a methylene group; or

8. cyclizing compounds of the formula XIII

$$W\text{-}N\text{-}(C_2H_4Q)_2 \qquad (XIII),$$

where W and Q are as defined above, with a compound of the formula XIV

$$NH_2\text{-}Ar \qquad (XIV),$$

where Ar is as defined above, to give compounds of the formula XV

$$W\text{-}B^1\text{-}Ar \qquad (XV).$$

The substances of the formulae III and V required as starting materials for synthesizing the novel compounds are known or can be prepared according to known processes (for example Organikum Barth Dt. Verl. der Wiss. 1993 or A. R. Katritzky, C. W. Rees (ed.) Comprehensive Heterocyclic Chemistry Pergamon Press) from analogous starting materials.

The further reaction of the compounds

$$H\text{-}B\text{-}Ar \qquad (III)$$

prepared in this manner according to 1. to 4. with subsequent removal of any protective groups to give the compounds of the formula V is carried out by attachment to compounds of the formula XVI

$$Q\text{-}A\text{-}Q' \qquad (XVI),$$

where Q and Q' are leaving groups, under conditions known per se.

The substances of the formulae II, IV, VI and of the formulae P-Ar, $NH_2$-Ar, W-$B^1$ or W-$B^2$-$P^1$ required as starting materials for synthesizing the novel compounds are known or can be prepared according to the preparation processes described in the

literature from analogous starting materials (for example B. Schulze, K. Illgen J. prakt. Chem. 1997, 339, 1 or K. Auer, E. Hungerbühler, R. W. Lang Chimia 1990, 44, 120 or A. Yokoo et al. Bull. Chem. Soc. Jpn. 1956, 29, 631 or L. Börjeson et al. Acta Chem. Chem. 1991, 45, 621 or Organikum Barth Dt. Verl. der Wiss. 1993 or A. R. Katritzky, C. W. Rees (ed.) Comprehensive Heterocyclic Chemistry Pergamon Press or The Chemistry of Heterocyclic Compounds J. Wiley & Sons Inc. NY and literature cited therein).

Example 1

3,3-Dimethyl-2-[3-(4-tetralin-5-yl-piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

Preparation of the starting materials

a) 3,3-Dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

The preparation of this compound was carried out in a manner known from the literature (K. Auer, E. Hungerbühler, R. W. Lang Chimia 1990, 44, 120). 3,3-Diethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 174°C) and 3,3-dimethyl-6-nitro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 187°C) were obtained in a similar manner.

b) 2-(3-Chloroprop-1-yl)-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

A solution of 5.9 g (3 mmol) of 3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide in 150 ml of DMF was initially charged at room temperature and, after addition of 3.7 g (3.3 mmol) of potassium t-butoxide, heated under nitrogen to 80°C. 14.2 g (9 mmol) of 1-bromo-3-chloropropane were then added quickly, and the mixture was stirred at 100°C for 30 min. The mixture was poured into ice-water and extracted with ether, and the organic phases were washed with water, dried with sodium sulfate and subsequently concentrated, so that the product precipitated out in crystalline form and could be filtered off with suction. This gave 6.7 g (82%) of substance. M.p.: 107°C.

2-(3-Chloroprop-1-yl)-3,3-diethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 70°C), 2-(3-chloroprop-1-yl)-3,3-dimethyl-6-nitro-2,3-dihydro-1,2- benzisothiazole 1,1-dioxide (m.p.: 146°C), 2-(2-chloroethyl)-3,3-diethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (oil), 2-(2-chloroethyl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

(oil), 2-(3-chloro-2-methyleneprop-1-yl)-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 115°C) and 2-(3-chloroprop-1-yl)-3,3-dimethyl-6-nitro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 146°C) were obtained in a similar manner.

c) 1-Tetralin-5-yl-piperazine

14.7 g (0.1 mol) of 5-aminotetraline and 18 g (0.11 mol) of bis(β-chloroethyl)amine hydrochloride in 300 ml of n-butanol were refluxed for 48 h, 5.4 g of sodium carbonate were added after cooling and the mixture was once more refluxed for 20 h. The precipitate which was formed by cooling was filtered off with suction, taken up in water and admixed with 2N sodium hydroxide solution. The aqueous phase was extracted with ethyl acetate, and the extract was washed with water, dried over sodium sulfate and concentrated under reduced pressure. In this manner, it was possible to isolate 10.7 g (50%) of the product as an oil.

4-Piperazin-1-ylisoquinoline

4.51 g (21.7 mmol) of 4-bromoisoquinoline, 4.65 g (25.0 mmol) of t-butyl piperazine-N-carboxylate, 0.1 g (0.11 mmol) of tris-(dibenzylideneacetone)dipalladium, 0.11 g (0.18 mmol) of 2,2'-bis(diphenylphosphino)-1,1'-dinaphthyl and 2.92 g (30.4 mmol) of sodium t-butoxide were admixed in 50 ml of toluene and stirred at 75°C for 2 h. The reaction mixture was poured onto ice/sodium chloride and extracted with ethyl acetate, the organic phase was dried over sodium sulfate and the solvent was removed using a rotary evaporator. The product crystallized out, and it was filtered off with suction and washed with pentane. This gave 5.5 g (81%) of the Boc-protected piperazine (m.p.: 111°C). 5.2 g (16.6 mmol) of this substance were taken up in 17 ml of dichloromethane and, at 0°C, slowly admixed with 17 ml (0.22 mol) of trifluoroacetic acid. The mixture was stirred at 0°C for 4 h, poured onto ice-water and extracted with dichloromethane. The aqueous phase was filtered, made alkaline and extracted with dichloromethane. After drying over sodium sulfate and substantial removal of the solvent, the residue was diluted with diethyl ether and the hydrochloride was precipitated out using ethereal hydrochloric acid. This gave 3.2 g (67%) of the product. (m.p.: 293°C).

The following compounds were prepared similarly to the two processes described: 1-naphth-1-yldiazepane (85°C, hydrochloride), 1-naphth-1-ylmethylpiperazine (oil), 4-piperazin-1-yl-indane (oil), 1-naphth-1-ylpiperazine (82°C), 4-chloro-1-piperazin-

1-ylphthalazine (205°C, decomp.) and 4-piperazin-1-ylquinazoline (320°C, hydrochloride). Other derivatives were commercially available.

Preparation of the end product

1.1 g (5.2 mmol) of 1-tetralin-5-ylpiperazine, 1.5 ml of triethylamine and a trace of potassium iodide were added to a solution of 1.64 g (6.0 mmol) of 2-(3-chloroprop-1-yl)-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide in 40 ml of DMF. The reaction mixture was allowed to react at 100°C for four hours and then poured onto ice-water, and the resulting precipitate was filtered off with suction. Purification was carried out by recrystallization from isopropanol, giving 1 g (43%) of the product (m.p.: 140°C).

NMR: $CDCl_3$ δ 7.8 (d, 1H), 7.6 (dd, 1H), 7.5 (dd, 1H), 7.4 (d, 1H), 7.1 (dd, 1H), 6.9 (d, 1H), 6.8 (d, 1H), 3.4 (t, 2H), 3.0-2.5 (m, 14H), 2.1 (tt, 2H), 1.8-1.7 (m, 4H), 1.5 (s, 6H) ppm.

The following compounds were obtained in a similar manner:

Example 2:
3,3-dimethyl-2-[3-(4-(2-phenylquinazolin-4-yl)piperazin-1-yl)-prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p.: 269°C, hydrochloride).

Example 3:
3,3-dimethyl-2-[3-(4-quinolin-2-yl-piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 63°C).

Example 4:
3,3-dimethyl-2-[3-(4-naphth-1-yl-1,4-diazepan-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 126°C, hydrochloride).

Example 5:
3,3-dimethyl-2-[3-(4-(4-chlorophthalazin-1-yl)piperazin-1-yl)-eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 190°C).

Example 6:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)-2-methyleneprop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 193°C).

Example 7:
3,3-dimethyl-2-[2-(4-quinazolin-4-ylpiperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 178°C, hydrochloride).

Example 8:
3,3-dimethyl-2-[2-(4-naphth-1-ylpiperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 282°C, hydrochloride).

Example 9:
3,3-dimethyl-2-[2-(4-isoquinolin-4-yl)piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 243°C, hydrochloride).

Example 10:
3,3-diethyl-2-[2-(4-naphth-1-yl-piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (oil).

Example 11:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-pyrrol-1-yl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 269°C, hydrochloride).

The pyrrole ring was constructed by reacting 3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-amino-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide with 2,5-dimethoxytetrahydrofuran in glacial acetic acid at 100°C (1h), in a yield of 86%.

Example 12:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-benzoylamido-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 127°C).

Example 13:
3,3-dimethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-6-nitro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 203°C).

Example 14:
3,3-dimethyl-2-[2-(4-(2,3-dimethylphenyl)piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 291°C, hydrochloride).

Example 15:
3,3-dimethyl-2-[2-(4-indan-4-ylpiperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 271°C, hydrochloride).

Example 16:
3,3-dimethyl-2-[3-(4-(4-chloronaphth-1-yl)piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 151°C).

Example 17:
3,3-dimethyl-2-[3-(4-pyrimidin-2-ylpiperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 263°C, hydrochloride).

Example 18:
3,3-dimethyl-2-[2-(4-(4-methoxyphenyl)-piperazin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 207°C, hydrochloride).

Example 19:
3,3-dimethyl-2-[3-(4-(2-methoxyphenyl)piperazin-1-yl)-2-hydroxy-prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 160°C).

Example 20:
3,3-diethyl-2-[3-(4-naphth-1-ylpiperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 179°C).

Example 21:
3,3-dimethyl-2-[3-(4-(2,5-dimethylphenyl)piperazin-1-yl)prop-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 218°C, hydrochloride).

Example 22:
3,3-dimethyl-2-[2-(4-(2-cyanophenyl)piperazin-1-yl)-eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide (m.p. 228°C, hydrochloride).

Example 23:
3,3-dimethyl-2-[2-(4-naphth-1-ylpiperazin-1-yl)eth-1-yl]-4-chloro-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

Preparation of the starting materials

a) 4-Chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide. This compound was prepared similarly to Example 1 a). Yield 7.8 g (70%). (m.p. 121°C)

b) 2-(2,2-Diethoxyeth-1-yl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

7.7 g (33 mmol) of 4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide, 8.25 ml (55 mmol) of bromoacetaldehyde diethyl acetal and 7.0 g of potassium carbonate were taken up in 100 ml of dry DMF and stirred at 120°C for 5 h. The reaction mixture was poured into ice-water and then extracted with ethyl acetate, and the organic phase was washed with water and dried over sodium sulfate. The solvent was removed under reduced pressure and the crude product was purified by column chromatography. This gave 7.5 g (65%) of the product as an oil.

c) 2-(2-Oxoeth-1-yl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

7.5 g (21.5 mmol) of 2-(2,2-diethoxyeth-1-yl)-4-chloro-3,3-dimethyl-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide and 25 ml of conc. hydrochloric acid were taken up in 25 ml of water and 150 ml of THF and stirred at 40°C for 1.5 h. The reaction mixture was neutralized using aqueous sodium hydroxide solution and extracted with ether, and the organic phase was dried over sodium sulfate and concentrated under reduced pressure. In this manner, it was possible to isolate 5.8 g (98%) of the product as an oil.

Preparation of the end product

1.5 g (5.5 mmol) of the aldehyde 24 c), 1.06 g (5 mmol) of naphthylpiperazine (prepared analogously to Example 1 c)) and 0.42 g (7 mmol) of glacial acetic acid were initially charged in 50 ml of ethanol, the mixture was stirred at room temperature for 30 minutes and 0.5 g (8 mmol) of sodium cyanoborohydride were then added slowly. The reaction mixture was stirred at room temperature for 2 h and then poured onto an ice/sodium chloride mixture and extracted with dichloromethane. The extract was dried with sodium sulfate, the solvent was distilled off and the residue was subsequently recrystallized from ethanol, giving 0.9 g (39%) of colorless crystals (m.p. 156°C).

NMR:$CDCl_3$ δ = 8.3 (m, 1H), 7.8 (m, 1H), 7.7 (d, 1H), 7.6 - 7.3 (m, 6H), 7.1 (d, 1H), 3.5 (t, 2H), 3.2 (m, 4H), 3.0 - 2.8 (m, 6H), 1.8 (s, 6H) ppm.

Example 24

Preparation of 3,3-dimethyl-2-[2-(4-naphth-1-yltetrahydro-1,2,3,6-pyridin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

Synthesis of the starting materials

a) N-Boc-4-(trifluoromethanesulfonyloxy)tetrahydro-1,2,3,6-pyridine

At -78°C, a solution of 13.2 g (0.13 mol) of diisopropylamine in 200 ml of THF was deprotonated with 100 ml of nBuLi (1.6M in hexane), and, after 30 minutes at this temperature, 20.0 g (0.1 mol) of N-Boc-piperidone, dissolved in 50 ml of THF, were added dropwise. After a further three hours at -78°C, a solution of 39.3 g (0.11 mol) of N,N-bistrifluoromethanesulfonylaniline in 50 ml of THF was added, and the reaction mixture was allowed to warm to room temperature overnight. For work-up, the mixture was admixed with water and extracted with ether, the organic phases were washed with $NaHCO_3$ solution and water and dried over sodium sulfate, and the solvent was concentrated. The crude product was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 3/1).
Yield: 20.2 g (60% of theory)
$^1H$ NMR:(270 MHz, $CDCl_3$) δ = 1.4 (s, 9H); 2.4 (m, 2H); 3.6 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H) ppm.

b) N-Boc-4-naphth-1-yltetrahydro-1,2,3,6-pyridine

14.7 g (44.4 mmol) of the compound described above, dissolved in 115 ml of dimethoxyethane, were admixed successively with 22 ml of 2M sodium carbonate solution, 7.63 g (44.4 mmol) of naphthyl-1-boronic acid, 4.13 g (97.6 mmol) of lithium chloride, 0.85 g (4.44 mmol) of copper(I) iodide and 2.1 g (1.77 mmol) of tetrakistriphenylpalladium, and the mixture was heated at the boil for 4 h. For work-up, aqueous ammonia solution was added to the mixture, which was then extracted with water and ethyl acetate, the extract was dried over sodium sulfate and the residue which was obtained after evaporation of the solvent was purified by flash chromatography (silica gel, mobile phase heptane/ethyl acetate = 4/1).
Yield: 8.2 g (57% of theory)

$^1$H NMR (270 MHz, $CDCl_3$): δ = 1.4 (s, 9H); 2.5 (m, 2H); 3.7 (t, 2H); 4.1 (m, 2H); 5.8 (m, 1H); 7.2-7.5 (m, 3H); 7.3-8.0 (m, 3H) ppm.

c) 4-Naphth-1-yltetrahydro-1,2,3,6-pyridine

7.84 g (25.3 mmol) of N-Boc-4-naphth-1-yl-3,6-dihydro-2H-pyridine were stirred overnight at room temperature with 200 ml of ethereal hydrochloric acid, and the precipitated product was filtered off and dried.
Yield: 5.5 g (88% of theory).

d) Preparation of the end product

1.0 g (4.1 mmol) of the compound 24c described above, dissolved in 20 ml of methanol, was, in the presence of 2.22 g (16.8 mmol) of zinc(II) chloride, admixed first with 1.27 g (5.3 mmol) of the aldehyde described under Example 23c and then with 0.5 g (8.14 mmol) of sodium cyanoborohydride. After 16 h at room temperature, the mixture was worked up as described and the resulting crude product was purified by chromatography (silica gel, mobile phase dichloromethane/methanol = 97/3). Precipitation of the salt using ethereal hydrochloric acid solution gave a white solid.
Yield: 0.9 g (47% of theory)
$^1$H NMR (270 MHz, DMSO-d6): δ = 1.6 (m, 6H); 2.6 (m, 1H); 3.1 (m, 1H); 3.4-3.6 (m, 6H); 4.0-4.2 (m, 2H); 5.8 (brd. s, 1H); 7.6-8.0 (m, 7H); 8.2 (d, 1H); 12.0 (s, 1H) ppm.

Example 25

Preparation of 3,3-dimethyl-2-[2-(4-naphth-1-ylpiperidin-1-yl)eth-1-yl]-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide

a) 4-Naphth-1-ylpiperidine

3.7 g (15.3 mmol) of 4-naphth-1-yltetrahydro-1,2,3,6-pyridine, dissolved in methanol, were hydrogenated with hydrogen for 48 h at room temperature, with addition of 0.8 g of palladium on carbon. The catalyst was filtered off and the solvent was concentrated.
Yield: 1.8 g (56% of theory)
$^1$H NMR (270 MHz, $CDCl_3$) δ = 1.6-1.8 (m, 2H); 2.0 (m, 2H); 2.9 (dt, 2H); 3.3 (d, 2H); 3.5 (tt, 1H); 7.4-7.6 (m, 4H); 7.7 (d, 1H); 7.9 (d, 1H); 8.1 (d, 1H) ppm.

Preparation of the end product

A solution of 1.5 g (7.1 mmol) of the amine 25a in 20 ml of methanol was admixed first with 3.8 g (28.4 mmol) of zinc chloride and then with 2.21 g (9.2 mmol) of the aldehyde described under Example 23 c, dissolved in 15 ml of methanol, and 0.89 g (14.2 mmol) of sodium cyanoborohydride was then added a little at a time. The mixture was stirred for six hours, undissolved particles were then filtered off, the mother liquor was concentrated and the residue was taken up in ethyl acetate. The organic phase was washed with water and saturated sodium chloride solution, dried over sodium sulfate and filtered, giving, on concentration, a yellowish oil.
Yield: 2.2 g (65% of theory)
$^1$H NMR (270 MHz, $CDCl_3$): $\delta$ = 1.7-1.9 (m, 8H); 2.0 (m, 2H); 2.7-3.0 (m, 4H); 3.2 (m, 2H); 3.5 (m, 1H); 3,7 (t, 2H); 7.1 (d, 1H); 7.3-7.7 (m, 9H); 8.2 (d, 1H) ppm.

Other preferred compounds of the formula I according to the invention are listed in the table below.

These compounds are suitable for preparing medicaments for the prophylaxis and therapy of neurodegeneration, cerebral trauma and cerebral ischemia, in particular stroke, and of diseases which are caused by these disorders.

A use according to the invention also relates to neuroprotection.

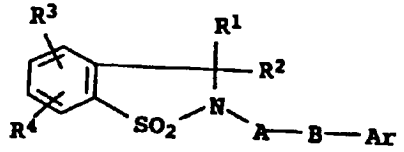
The preparation of these compounds is described in the patents mentioned at the outset.

The preparation as a medicament is carried out using a compound of the formula I or its pharmacologically acceptable acid addition salt as active compound, together with customary excipients and diluents.

The use according to the invention can be carried out in a customary manner, orally or parenterally, intravenously or intramuscularly.

The dosage depends on the age, on the state and the weight of the patient and on the type of administration. In general, the daily dose of active compound is between approximately 1 and 100 mg/kg of body weight in the case of oral administration and between 0.1 and 10 mg/kg of body weight in the case of parenteral administration.

The medicaments can be used in solid or liquid form in customary pharmaceutical administration forms, for example as tablets, film-coated tablets, capsules, powders, granules, sugar-coated tablets, suppositories, solutions, ointments, creams or sprays. These are prepared in a customary manner. Here, the active compounds can be processed with the customary pharmaceutical auxiliaries, such as tablet binders, fillers, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, sustained-release agents, antioxidants and/or propellants (cf. H. Sucker et al.: Pharmazeutische Technologie [Pharmaceutical Technology], Thieme-Verlag, Stuttgart, 1978). The resulting administration forms generally comprise the active compound in an amount of from 1 to 99% by weight.



I

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 26 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 9-anthracene | 178°C (HCl) |
| 27 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe-1-naphthaline | 181°C (HCl) |
| 28 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 1-naphthaline | >250°C (HCl) |
| 29 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-pyridine | 135°C (HCl) |
| 30 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$CH_3$-2-pyridine | 128°C |
| 31 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Ph-4-quinazoline | 172°C |
| 32 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$CF_3$-2-pyridine | 138°C |
| 33 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-pyrimidine | 124°C |
| 34 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-Cl-1-Phthalazin | 190°C (HCl) |
| 35 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 5-tetra-lin | 275°C (HCl) |
| 36 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$CF_3$-Ph | 265°C (HCl) |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 37 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-$NO_2$-Ph | 152°C |
| 38 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Me-Ph | |
| 39 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OH-Ph | |
| 40 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Br-Ph | |
| 41 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-$CF_3$-Ph | |
| 42 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OEt-Ph | |
| 43 | Me | H | H | Me | Me | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$-Ph | |
| 44 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-O(n-$C_4$)-Ph | |
| 45 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-F-Ph | |
| 46 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe-Ph | |
| 47 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Cl-Ph | |
| 48 | Me | H | H | / | / | H | $C_2$ | 4-piperazine-1-yl | 2-$CO_2R^7$-Ph | |
| 49 | Me | H | H | / | / | Me | $C_2$ | 4-piperazine-1-yl | 2-$CO_2R^7$-Ph | |
| 50 | Me | H | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$-Ph | |
| 51 | Me | H | H | n-$C_3$ | n-$C_3$ | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$-Ph | |
| 52 | Me | H | H | i-$C_3$ | i-$C_3$ | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$-Ph | |
| 53 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-I-Ph | |
| 54 | Me | H | H | / | / | i-$C_3$ | $C_2$ | 4-piperazine-1-yl | 2-$CO_2R^7$-Ph | |
| 55 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | Ph | |
| 56 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Et-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 57 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-i$C_3$-Ph | |
| 58 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Ph-Ph | |
| 59 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-tBu-Ph | |
| 60 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Et-Ph | |
| 61 | Me | H | H | / | / | Et | $C_2$ | 4-piperazine-1-yl | 3-$CO_2R^7$-Ph | |
| 62 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-I-Ph | |
| 63 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Cl-Ph | |
| 64 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Br-Ph | |
| 65 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-F-Ph | |
| 66 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-OH-Ph | |
| 67 | Me | H | H | / | / | H | $C_2$ | 4-piperazine-1-yl | 3-$CO_2R^7$-Ph | |
| 68 | Me | H | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 3-$NR^5R^6$-Ph | |
| 69 | Me | H | H | Me | Me | / | $C_2$ | 4-piperazine-1-yl | 3-$NR^5R^6$-Ph | |
| 70 | Me | H | H | i-$C_3$ | i-$C_3$ | / | $C_2$ | 4-piperazine-1-yl | 3-$NR^5R^6$-Ph | |
| 71 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-CN-Ph | |
| 72 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-OMe-Ph | |
| 73 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$NO_2$-Ph | |
| 74 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-OEt-Ph | |
| 75 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-O(n-$C_5$)Ph | |
| 76 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-Ph-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 77 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-$iC_3$-Ph | |
| 78 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-$nC_3$-Ph | |
| 79 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-$nC_6$-Ph | |
| 80 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-I-Ph | |
| 81 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-F-Ph | |
| 82 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-Br-Ph | |
| 83 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-Cl-Ph | |
| 84 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-OH-Ph | |
| 85 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-CN-Ph | |
| 86 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-$CF_3$-Ph | |
| 87 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-$NO_2$-Ph | |
| 88 | Me | H | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 4-$NR^5R^6$-Ph | |
| 89 | Me | H | H | Me | Me | / | $C_2$ | 4-piperazine-1-yl | 4-$NR^5R^6$-Ph | |
| 90 | Me | H | H | n-$C_4$ | n-$C_4$ | / | $C_2$ | 4-piperazine-1-yl | 4-$NR^5R^6$-Ph | |
| 91 | Me | H | H | Me | Et | / | $C_2$ | 4-piperazine-1-yl | 4-$NR^5R^6$-Ph | |
| 92 | Me | H | H | / | / | H | $C_2$ | 4-piperazine-1-yl | 4-$CO_2R^7$-Ph | |
| 93 | Me | H | H | / | / | Me | $C_2$ | 4-piperazine-1-yl | 4-$CO_2R^7$-Ph | |
| 94 | Me | H | H | / | / | n-$C_5$ | $C_2$ | 4-piperazine-1-yl | 4-$CO_2R^7$-Ph | |
| 95 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-OEt-Ph | |
| 96 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Cl,4-$NO_2$-Ph | |



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| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 97 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Cl,4-Me-Ph | |
| 98 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-CN,6-CN-Ph | |
| 99 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Me,6-Me-Ph | |
| 100 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-$NO_2$,4-$CF_3$-Ph | |
| 101 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Cl,4-Cl-Ph | |
| 102 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Et,3-Et-Ph | |
| 103 | Me | H | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |
| 104 | Me | H | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$,4-Me-Ph | |
| 105 | Me | H | H | Me | Me | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |
| 106 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Me,4-Me-Ph | |
| 107 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Cl,5-Cl-Ph | |
| 108 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,4-OMe-Ph | |
| 109 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-tBu,5-tBu-Ph | |
| 110 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-tBu,5-$CF_3$-Ph | |
| 111 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,5-Cl-Ph | |
| 112 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,5-OMe-Ph | |
| 113 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,5-Ph-Ph | |
| 114 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,4-OMe-Ph | |
| 115 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$CF_3$,4-Cl-Ph | |
| 116 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-$NO_2$,4-$CF_3$,5-$NO_2$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 117 | Me | H | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 2-$NR^5R^6$,4-Me,5-Cl-Ph | |
| 118 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,3-Cl,5-Cl-Ph | |
| 119 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,4-$NO_2$,5-Me-Ph | |
| 120 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe,4-Cl,5-Me-Ph | |
| 121 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Me,4-Cl,5-$CF_3$-Ph | |
| 122 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-tetra-lin | |
| 123 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Indan | |
| 124 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe-1-naphthaline | |
| 125 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OEt-1-naphthaline | |
| 126 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Me-1-naphthaline | |
| 127 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Et-1-naphthaline | |
| 128 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 8-OMe-1-naphthaline | |
| 129 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 8-Me-1-naphthaline | |
| 130 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 9-anthracene | |
| 131 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Indol | |
| 132 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-quinazoline | |
| 133 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Chinoxalin | |
| 134 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Phthalazin | |
| 135 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-quinoline | |
| 136 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-quinoline | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 137 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 5-quinoline | |
| 138 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Isoquinoline | |
| 139 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 8-Isoquinoline | |
| 140 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 7-benzofuran | |
| 141 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-2H-chromene | |
| 142 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 5-chromane | |
| 143 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 8-chromane | |
| 144 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-pyrimidine | |
| 145 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 4-pyrimidine | |
| 146 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Pyrazin | |
| 147 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-Isoxazol | |
| 148 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-pyrrole | |
| 149 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 6-i$C_3$-4-pyrimidine | |
| 150 | Me | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 7-OMe-1-naphthaline | |
| 151 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Me-Ph | |
| 152 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OH-Ph | |
| 153 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Br-Ph | |
| 154 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-$CF_3$-Ph | |
| 155 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OEt-Ph | |
| 156 | Me | H | H | Me | Me | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 157 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-O(n-$C_4$)-Ph | |
| 158 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-$NO_2$-Ph | |
| 159 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-F-Ph | |
| 160 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe-Ph | |
| 161 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-CN-Ph | |
| 162 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Cl-Ph | |
| 163 | Me | H | H | / | / | H | $C_2$ | 4-piperidine-1-yl | 2-$CO_2R^7$-Ph | |
| 164 | Me | H | H | / | / | Me | $C_2$ | 4-piperidine-1-yl | 2-$CO_2R^7$-Ph | |
| 165 | Me | H | H | H | H | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$-Ph | |
| 166 | Me | H | H | n-$C_3$ | n-$C_3$ | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$-Ph | |
| 167 | Me | H | H | i-$C_3$ | i-$C_3$ | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$-Ph | |
| 168 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-I-Ph | |
| 169 | Me | H | H | / | / | i-$C_3$ | $C_2$ | 4-piperidine-1-yl | 2-$CO_2R^7$-Ph | |
| 170 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | Ph | |
| 171 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Et-Ph | |
| 172 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-i$C_3$-Ph | |
| 173 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Ph-Ph | |
| 174 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-tBu-Ph | |
| 175 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Et-Ph | |
| 176 | Me | H | H | / | / | Et | $C_2$ | 4-piperidine-1-yl | 3-$CO_2R^7$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 177 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-I-Ph | |
| 178 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Cl-Ph | |
| 179 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Br-Ph | |
| 180 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-F-Ph | |
| 181 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-$CF_3$-Ph | |
| 182 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-OH-Ph | |
| 183 | Me | H | H | / | / | H | $C_2$ | 4-piperidine-1-yl | 3-$CO_2R^7$-Ph | |
| 184 | Me | H | H | H | H | / | $C_2$ | 4-piperidine-1-yl | 3-$NR^5R^6$-Ph | |
| 185 | Me | H | H | Me | Me | / | $C_2$ | 4-piperidine-1-yl | 3-$NR^5R^6$-Ph | |
| 186 | Me | H | H | i-$C_3$ | i-$C_3$ | / | $C_2$ | 4-piperidine-1-yl | 3-$NR^5R^6$-Ph | |
| 187 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-CN-Ph | |
| 188 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-OMe-Ph | |
| 189 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-$NO_2$-Ph | |
| 190 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-OEt-Ph | |
| 191 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-O(n-$C_5$)Ph | |
| 192 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-Ph-Ph | |
| 193 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-i$C_3$-Ph | |
| 194 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-n$C_3$-Ph | |
| 195 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-n$C_6$-Ph | |
| 196 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-I-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 197 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-F-Ph | |
| 198 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-Br-Ph | |
| 199 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-Cl-Ph | |
| 200 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-OH-Ph | |
| 201 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-CN-Ph | |
| 202 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-$CF_3$-Ph | |
| 203 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-$NO_2$-Ph | |
| 204 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-$NR^5R^6$-Ph | |
| 205 | Me | H | H | Me | Me | / | $C_2$ | 4-piperidine-1-yl | 4-$NR^5R^6$-Ph | |
| 206 | Me | H | H | n-$C_4$ | n-$C_4$ | / | $C_2$ | 4-piperidine-1-yl | 4-$NR^5R^6$-Ph | |
| 207 | Me | H | H | Me | Et | / | $C_2$ | 4-piperidine-1-yl | 4-$NR^5R^6$-Ph | |
| 208 | Me | H | H | / | / | H | $C_2$ | 4-piperidine-1-yl | 4-$CO_2R^7$-Ph | |
| 209 | Me | H | H | / | / | Me | $C_2$ | 4-piperidine-1-yl | 4-$CO_2R^7$-Ph | |
| 210 | Me | H | H | / | / | n-$C_5$ | $C_2$ | 4-piperidine-1-yl | 4-$CO_2R^7$-Ph | |
| 211 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-OMe-Ph | |
| 212 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-OEt-Ph | |
| 213 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Cl,4-$NO_2$-Ph | |
| 214 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Cl,4-Me-Ph | |
| 215 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-CN,6-CN-Ph | |
| 216 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Me,6-Me-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 217 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-$NO_2$,4-$CF_3$-Ph | |
| 218 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Cl,4-Cl-Ph | |
| 219 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Me,3-Me-Ph | |
| 220 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Et,3-Et-Ph | |
| 221 | Me | H | H | H | H | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |
| 222 | Me | H | H | H | H | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |
| 223 | Me | H | H | Me | Me | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |
| 224 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Me,4,Me-Ph | |
| 225 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Cl,5-Cl-Ph | |
| 226 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,4-OMe-Ph | |
| 227 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-tBu,5-tBu-Ph | |
| 228 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-tBu,5-$CF_3$-Ph | |
| 229 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,5-Cl-Ph | |
| 230 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,5-OMe-Ph | |
| 231 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,5-Ph-Ph | |
| 232 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-OMe,4-OMe-Ph | |
| 233 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-$CF_3$,4-Cl-Ph | |
| 234 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-$NO_2$,4-$CF_3$,5-$NO_2$-Ph | |
| 235 | Me | H | H | H | H | / | $C_2$ | 4-piperidine-1-yl | 2-$NR^5R^6$,4-Me,5-Cl-Ph | |
| 236 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,3-Cl,5-Cl-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 237 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,4-$NO_2$,5-Me-Ph | |
| 238 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe,4-Cl,5-Me-Ph | |
| 239 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Me,4-Cl,5-$CF_3$-Ph | |
| 240 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 5-tetra-lin | |
| 241 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-Indan | |
| 242 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 1-tetra-lin | |
| 243 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 1-Indan | |
| 244 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OMe-1-naphthaline | |
| 245 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-OEt-1-naphthaline | |
| 246 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Me-1-naphthaline | |
| 247 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Et-1-naphthaline | |
| 248 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 8-OMe-1-naphthaline | |
| 249 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 8-Me-1-naphthaline | |
| 250 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 9-anthracene | |
| 251 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Indol | |
| 252 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-quinazoline | |
| 253 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-quinazoline | |
| 254 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Chinoxalin | |
| 255 | Me | H | H | / | / | ( | $C_2$ | 4-piperidine-1-yl | 1-Phthalazin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 256 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-quinoline | |
| 257 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-quinoline | |
| 258 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-quinoline | |
| 259 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 5-quinoline | |
| 260 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 1-Isoquinoline | |
| 261 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-Isoquinoline | |
| 262 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 8-Isoquinoline | |
| 263 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 7-benzofuran | |
| 264 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-2H-chromene | |
| 265 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 5-chromane | |
| 266 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 8-chromane | |
| 267 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-pyrimidine | |
| 268 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | pyrimidine | |
| 269 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 5-OMe-4-pyrimidine | |
| 270 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 4-pyrimidine | |
| 271 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Pyrazin | |
| 272 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-Isoxazol | |
| 273 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-pyridine | |
| 274 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-pyridine | |
| 275 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 3-pyrrole | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 276 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 2-Ph-4-quinazoline | |
| 277 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 6-i$C_3$-4-pyrimidine | |
| 278 | Me | H | H | / | / | / | $C_2$ | 4-piperidine-1-yl | 7-OMe-1-naphthaline | |
| 279 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine | 2-Me-Ph | |
| 280 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OH-Ph | |
| 281 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Br-Ph | |
| 282 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$CF_3$-Ph | |
| 283 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OEt-Ph | |
| 284 | Me | H | H | Me | Me | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$-Ph | |
| 285 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-O(n-$C_4$)-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 286 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NO_2$-Ph | |
| 287 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-F-Ph | |
| 288 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe-Ph | |
| 289 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-CN-Ph | |
| 290 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Cl-Ph | |
| 291 | Me | H | H | / | / | H | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$CO_2R^7$-Ph | |
| 292 | Me | H | H | / | / | Me | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$CO_2R^7$-Ph | |
| 293 | Me | H | H | H | H | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 294 | Me | H | H | n-$C_3$ | n-$C_3$ | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$-Ph | |
| 295 | Me | H | H | i-$C_3$ | i-$C_3$ | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$-Ph | |
| 296 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-I-Ph | |
| 297 | Me | H | H | / | / | i-$C_3$ | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$CO_2R^7$-Ph | |
| 298 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | Ph | |
| 299 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Et-Ph | |
| 300 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-i$C_3$-Ph | |
| 301 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Ph-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 302 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-tBu-Ph | |
| 303 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Et-Ph | |
| 304 | Me | H | H | / | / | Et | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$CO_2R^7$-Ph | |
| 305 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-I-Ph | |
| 306 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Cl-Ph | |
| 307 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Br-Ph | |
| 308 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-F-Ph | |
| 309 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$CF_3$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 310 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-OH-Ph | |
| 311 | Me | H | H | / | / | H | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$CO_2R^7$-Ph | |
| 312 | Me | H | H | H | H | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$NR^5R^6$-Ph | |
| 313 | Me | H | H | Me | Me | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$NR^5R^6$-Ph | |
| 314 | Me | H | H | i-$C_3$ | i-$C_3$ | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$NR^5R^6$-Ph | |
| 315 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-CN-Ph | |
| 316 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-OMe-Ph | |
| 317 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$NO_2$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 318 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-OEt-Ph | |
| 319 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-O(n-$C_5$)Ph | |
| 320 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-Ph-Ph | |
| 321 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-i$C_3$-Ph | |
| 322 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-n$C_3$-Ph | |
| 323 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-n$C_6$-Ph | |
| 324 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-I-Ph | |
| 325 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-F-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 326 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-Br-Ph | |
| 327 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-Cl-Ph | |
| 328 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-OH-Ph | |
| 329 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-CN-Ph | |
| 330 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$CF_3$-Ph | |
| 331 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$NO_2$-Ph | |
| 332 | Me | H | H | H | H | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$NR^5R^6$-Ph | |
| 333 | Me | H | H | Me | Me | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$NR^5R^6$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 334 | Me | H | H | n-$C_4$ | n-$C_4$ | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$NR^5R^6$-Ph | |
| 335 | Me | H | H | Me | Me | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$NR^5R^6$-Ph | |
| 336 | Me | H | H | / | / | H | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$CO_2R^7$-Ph | |
| 337 | Me | H | H | / | / | Me | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$CO_2R^7$-Ph | |
| 338 | Me | H | H | / | / | n-$C_5$ | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-$CO_2R^7$-Ph | |
| 339 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-OMe-Ph | |
| 340 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-OEt-Ph | |
| 341 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Cl,4-$NO_2$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 342 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Cl,4-Me-Ph | |
| 343 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-CN,6-CN-Ph | |
| 344 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Me,6-Me-Ph | |
| 345 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NO_2$,4-$CF_3$-Ph | |
| 346 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Cl,4-Cl-Ph | |
| 347 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Me,3-Me-Ph | |
| 348 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Et,3-Et-Ph | |
| 349 | Me | H | H | H | H | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 350 | Me | H | H | H | H | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$,4-Me-Ph | |
| 351 | Me | H | H | Me | Me | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$,4-Cl-Ph | |
| 352 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Me,4-Me-Ph | |
| 353 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Cl,5-Cl-Ph | |
| 354 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,4-OMe-Ph | |
| 355 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-tBu,5-tBu-Ph | |
| 356 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-tBu,5-$CF_3$-Ph | |
| 357 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,5-Cl-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 358 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,5-OMe-Ph | |
| 359 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,5-Ph-Ph | |
| 360 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,4-OMe-Ph | |
| 361 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-$CF_3$,4-Cl-Ph | |
| 362 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NO_2$,4-$CF_3$,5-$NO_2$-Ph | |
| 363 | Me | H | H | H | H | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-$NR^5R^6$,4-Me,5-Cl-Ph | |
| 364 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,3-Cl,5-Cl-Ph | |
| 365 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,4-$NO_2$,5-Me-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 366 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OMe,4-Cl,5-Me-Ph | |
| 367 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Me,4-Cl,5-$CF_3$-Ph | |
| 368 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-tetra-lin | |
| 369 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-Indan | |
| 370 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 1-tetra-lin | |
| 371 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 1-Indan | |
| 372 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-OEt-1-naphthaline | |
| 373 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Me-1-naphthaline | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 374 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Et-1-naphthaline | |
| 375 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 8-OMe-1-naphthaline | |
| 376 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 8-Me-1-naphthaline | |
| 377 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Indol | |
| 378 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-quinazoline | |
| 379 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-quinazoline | |
| 380 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Chinoxalin | |
| 381 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 1-Phthalazin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 382 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-quinoline | |
| 383 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-quinoline | |
| 384 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-quinoline | |
| 385 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 5-quinoline | |
| 386 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 1-Isoquinoline | |
| 387 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-Isoquinoline | |
| 388 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 8-Isoquinoline | |
| 389 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 7 Benzoferan | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 390 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-2H-chromene | |
| 391 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 5-chromane | |
| 392 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 8-chromane | |
| 393 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-pyrimidine | |
| 394 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | pyrimidine | |
| 395 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 5-OMe-4-pyrimidine | |
| 396 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 4-pyrimidine | |
| 397 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Pyrazin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | m.p. MS $^1$H-NMR |
|---|---|---|---|---|---|---|---|---|---|---|
| 398 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-Isoxazol | |
| 399 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-pyridine | |
| 400 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-pyridine | |
| 401 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 3-pyrrole | |
| 402 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 2-Ph-4-quinazoline | |
| 403 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 6-i$C_3$-4-pyrimidine | |
| 404 | Me | H | H | / | / | / | $C_2$ | 4-tetra-hydro-1,2,3,6 pyridine-1-yl | 7-OMe-1-naphthaline | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 405 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-Me-Ph | 137°C |
| 406 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-OMe-Ph | 233°C (HCl) |
| 407 | Me | H | H | H | H | / | $C_3$ | 4-piperazine-1-yl | 4-OMe-Ph | 237°C (HCl) |
| 408 | Me | H | H | / | / | Me | $C_3$ | 4-piperazine-1-yl | 3-OMe, 4-OMe-Ph | 224°C (HCl) |
| 409 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-pyrimidine | > 265°C (HCl) |
| 410 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 3-$NO_2$, 6-$OCH_3$-Ph | $^1$H-NMR (DMSO-$d_6$) δ= 1.5(6H,s), 3.3(3H,s) |
| 411 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 3-$NH_2$, 6-$OCH_3$-Ph | $^1$H-NMR (DMSO-$d_6$) δ= 1.5(6H,s), 3.4(3H,s) |
| 412 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 3-$OCH_3$-Ph | 179°C (HCl) |
| 413 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | quinazoline | 271°C (HCl) |
| 414 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 4-isoquinoline | 138°C |
| 415 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-thiazole | 217°C (HCl) |
| 416 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-Me, 5-Me-Ph | 98°C (HCl) |
| 417 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-Me,3-Me-Ph | 132°C |
| 418 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 3-Me, 4-Me-Ph | 124°C |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 419 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 1-naphthaline | 178°C |
| 420 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 4-Cl-1-naphthaline | 152°C |
| 421 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 2-pyrimidine3-$CF_3$_Ph | 196°C (HCl) |
| 422 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 1-isoquinoline | 63°C |
| 423 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-piperazine-1-yl | 3-$CF_3$-Ph | 184°C (HCl) |
| 424 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-piperazine-1-yl | 5-tetraline | $CH_2$-C($CH_2$)-C$H_2$177°C |
| 425 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-piperazine-1-yl | 4-indane | $CH_2$-C($CH_2$)-C$H_2$156°C |
| 426 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-piperazine-1-yl | 1-naphthaline | 177°C |
| 427 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-piperazine-1-yl | 2-$OCH_3$_Ph | 160°C |
| 428 | Me | H | H | / | / | / | $CH_2$-CH($CH_3$)-$CH_2$ | 3-$CF_3$-Ph | 5-Tetralin | 155°C (HCl) |
| 429 | Me | H | H | / | / | / | $C_4$ | 4-piperazine-1-yl | 2-pyrimidine | 220°C (HCl) |
| 430 | Me | 6-$NR^5R^6$ | H | H | H | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | 183°C |
| 431 | Me | 6-$NR^5R^6$ | H | COPh | H | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | 127°C |
| 432 | Me | 6-$NR^5R^6$ | H | COMe | H | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | 197°C |
| 433 | Me | 6-$NR^5R^6$ | H | Pyrrol | | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | 269°C (HCl) |
| 434 | Me | 6-$NO_2$ | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | 183°C |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 435 | Et | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$CF_3$-Ph | 277°C (HCl) |
| 436 | Et | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | 176°C |
| 437 | Prop | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 3-$CF_3$-Ph | 107°C |
| 438 | Prop | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 3-$CF_3$-Ph | 96°C (HCl) |
| 439 | Et | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 3-$CF_3$-Ph | 235°C (HCl) |
| 440 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Me-Ph | |
| 441 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-OH-Ph | |
| 442 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Br-Ph | |
| 443 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-$CF_3$-Ph | |
| 444 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-OMe-Ph | |
| 445 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-CN-Ph | |
| 446 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | Ph | |
| 447 | Me | H | H | H | H | / | $C_2$ | 4-Homopiperazine-1-yl | 2-$NR^5R^6$-Ph | |
| 448 | Me | H | H | Me | Me | / | $C_2$ | 4-Homopiperazine-1-yl | 2-$NR^5R^6$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 449 | Me | H | H | / | / | H | $C_2$ | 4-Homopiperazine-1-yl | 2-$CO_2R^7$-Ph | |
| 450 | Me | H | H | / | / | Me | $C_2$ | 4-Homopiperazine-1-yl | 2-$CO_2R^7$-Ph | |
| 451 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-tBu-Ph | |
| 452 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-Me-Ph | |
| 453 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-$CF_3$-Ph | |
| 454 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-Cl-Ph | |
| 455 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-OMe-Ph | |
| 456 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 4-$NO_2$-Ph | |
| 457 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 4-Ph-Ph | |
| 458 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 4-F-Ph | |
| 459 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-Cl,4-Me-Ph | |
| 460 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Me,6-Me-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 461 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Me,3-Me-Ph | |
| 462 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Et,3,-Et-Ph | |
| 463 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3t-Bu,5-$CF_3$-Ph | |
| 464 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-OMe,5-Ph-Ph | |
| 465 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-OMe,4-Cl,5-Me-Ph | |
| 466 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Me,4-Cl,5-$CF_3$-Ph | |
| 467 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 5-Tetralin | |
| 468 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 4-Indan | |
| 469 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 1-Naphthalin | |
| 470 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-OMe-1Naphthalin | |
| 471 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Me-1Naphthalin | |
| 472 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 7-OMe-1-Naphthalin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 473 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 8-Me-1-Naphthalin | |
| 474 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-quinazoline | |
| 475 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-Indol | |
| 476 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 1-Phthalazin | |
| 477 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Chinolin | |
| 478 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 1-Isoquinoline | |
| 479 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-pyrimidine | |
| 480 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 4-Isoquinoline | $[M+H]^+$=451 |
| 481 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 3-Isoquinoline $^1H$- | NMR(DMSO-$d_6$) $\delta$=1.5 (6H,s), 8.7 (1H,d) |
| 482 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | pyrimidine | |
| 483 | Me | H | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Pyridin | |
| 484 | Me | H | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 4-Indan | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 485 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 2-Me-Ph | |
| 486 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 2-OMe-Ph | |
| 487 | Me | H | H | H | H | / | $C_3$ | 4-Piperidin-1-yl | 2-$NR^5R^6$-Ph | |
| 488 | Me | H | H | / | / | Me | $C_3$ | 4-Piperidin-1-yl | 2-$CO_2R^7$-Ph | |
| 489 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 3-tBu-Ph | |
| 490 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 2-Me,3-Me-Ph | |
| 491 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 492 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 4-Indan | |
| 493 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 1-Naphthalin | |
| 494 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 2-Me-1-Naphtha-lin | |
| 495 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 2-pyrimidine | |
| 496 | Me | H | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 1-Phthalazin | |
| 497 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-Me-Ph | |
| 498 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-OMe-Ph | |
| 499 | Me | H | H | H | H | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-$NR^5R^6$-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 500 | Me | H | H | / | / | Me | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-$CO_2R^7$-Ph | |
| 501 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 3-tBu-Ph | |
| 502 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-Me,3-Me-Ph | |
| 503 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 5-Tetralin | |
| 504 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 4-Indan | |
| 505 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 1-Naphthalin | |
| 506 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-Me-1-Naphthalin | |
| 507 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 2-pyrimidine | |
| 508 | Me | H | H | / | / | / | $C_3$ | 4-Tetrahydro-1,2,3,6-pyridin-1-yl | 1-Phthalazin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 509 | Me | H | H | / | / | / | $C_3$ | 4-Homopiperazine-1-yl | 2-Me-Ph | |
| 510 | Me | H | H | / | / | / | $C_3$ | 4-Homopiperazine-1-yl | 2-Me,3-Me-Ph | |
| 511 | Me | H | H | / | / | / | $C_3$ | 4-Homopiperazine-1-yl | 5-Tetralin | |
| 512 | Me | H | H | / | / | / | $C_3$ | 4-Homopiperazine-1-yl | 2-Me-1-Naphthalin | |
| 513 | Me | H | H | / | / | / | $C_3$ | 4-Homopiperazine-1-yl | 2-pyrimidine | |
| 514 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-piperazine-1-yl | 2-Me, 3-Me-Ph | |
| 515 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-piperazine-1-yl | 2-OMe-1-Naphthalin | |
| 516 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-piperazine-1-yl | 2-pyrimidine | |
| 517 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 2-Me-Ph | |
| 518 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 2-Me, 3-Me-Ph | |
| 519 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 520 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 1-Naphthalin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 521 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 2-OMe-1-Naphthalin | |
| 522 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 2-pyrimidine | |
| 523 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Piperidin-1-yl | 2-Chinolin | |
| 524 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 2-Me-Ph | |
| 525 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 2-Me, 3-Me-Ph | |
| 526 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 5-Tetralin | |
| 527 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 1-Naphthalin | |
| 528 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 2-OMe-1-Naphthalin | |
| 529 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 2-pyrimidine | |
| 530 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Tetrahydropyridin-1-yl | 2-Chinolin | |
| 531 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Homopiperazine-1-yl | 2-Me-Ph | |
| 532 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Homopiperazine-1-yl | 2Me, 3-Me-Ph | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 533 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Hompoipera-zin-1-yl | 5-Tetralin | |
| 534 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Homopiperazine-1-yl | 1-Naphthalin | |
| 535 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Homopiperazine-1-yl | 2-OMe-1-Naphtha-lin | |
| 536 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Homopiperazine-1-yl | 2-pyrimidine | |
| 537 | Me | H | H | / | / | / | $CH_2$-C($CH_2$)-$CH_2$ | 4-Homopiperazine-1-yl | 2-Chinolin | |
| 538 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-piperazine-1-yl | 2-Me-Ph | |
| 539 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-piperazine-1-yl | 2-Me, 3-Me-Ph | |
| 540 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-piperazine-1-yl | 5-Tetralin | |
| 541 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-Piperidin-1-yl | 2-OMe-1-Naphtha-lin | |
| 542 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-Tetrahydropyi-din-1-yl | 2-pyrimidine | |
| 543 | Me | H | H | / | / | / | $CH_2$-CH(OH)-$CH_2$ | 4-Homopiperazine-1-yl | 2-Chinolin | |
| 544 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-piperazine-1-yl | 2-Me-Ph | |
| 545 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-piperazine-1-yl | 2-Me, 3-Me-Ph | |
| 546 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-piperazine-1-yl | 5-Tetralin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 547 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 548 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-Piperidin-1-yl | 2-OMe-1-Naphthalin | |
| 549 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-Tetrahydropyridin-1-yl | 2-pyrimidine | |
| 550 | Me | H | H | / | / | / | $C_2$-N(Me)-$C_2$ | 4-Homopiperazine-1-yl | 2-Chinolin | |
| 551 | Me | H | H | / | / | / | $CH_2$-$CH(CH_3)$-$CH_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 552 | Me | H | H | / | / | / | $CH_2$-$CH(CH_3)$-$CH_2$ | 4-Piperidin-1-yl | 2-Me, 3-Me-Ph | |
| 553 | Me | H | H | / | / | / | $CH_2$-$CH(CH_3)$-$CH_2$ | 4-Tetrahydropyridin-1-yl | 2-pyrimidine | |
| 554 | Me | H | H | / | / | / | $CH_2$-$CH(CH_3)$-$CH_2$ | 4-Homopiperazine-1-yl | 2-OMe-Naphthalin | |
| 555 | Me | 5-Me | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 5-Tetralin | |
| 556 | Me | 5-Me | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 557 | Me | 5-Me | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe-Ph | |
| 558 | Me | 5-Me | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-pyrimidine | |
| 559 | Me | 5-Me | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe-Naphthalin | |
| 560 | Me | 5-Me | H | / | / | / | $C_2$ | 4-Piperidin-1-yl | 2-Me,3-Me-Ph | |
| 561 | Me | 5-Me | H | / | / | / | $C_2$ | 4-Tetrahydropyridin-1-yl | 2-Chinolin | |

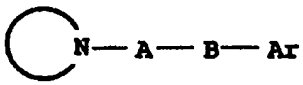
| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 562 | Me | 5-Me | H | / | / | / | $C_2$ | 4-Homopiperazine-1-yl | 2-Cl-Ph | |
| 563 | Me | 5-Me | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 5-Tetralin | |
| 564 | Me | 5-Me | H | / | / | / | $C_3$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 565 | Me | 5-Me | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 2-pyrimidine | |
| 566 | Me | 5-Me | H | / | / | / | $C_3$ | 4-Tetrahydropyridin-1-yl | 2-Me,3Me Ph | |
| 567 | Me | 5-Me | H | / | / | / | $C_3$ | 4-Homopiperazine-1-yl | 2-OMe-Naphthalin | |
| 568 | Me | 5-OH | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 569 | Me | 6-OMe | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 570 | Me | 4-F | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 571 | Me | 6-OMe | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 572 | Me | 4-$CF_3$ | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 573 | Me | 6-$CO_2R^7$ | H | / | / | H | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 574 | Me | 6-$CO_2R^7$ | H | / | / | Me | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 575 | Me | 4-CN | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 576 | Me | 4(-$C_2$-Ph) | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 577 | Me | 4[-$C_4$-(4-Cl)-Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 578 | Me | 4[-$C_2$-(2-OMe)Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 579 | Me | 4[$C_2$-(3-$CF_3$)Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 580 | Me | 4[$C_2$-(2-Me)Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 581 | Me | 4[$C_2$-(2-$NH_2$)Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 582 | Me | 4[$C_2$-(4-$NO_2$)Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 583 | Me | 4[$C_2$-(4-OH)Ph] | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 584 | Me | 6-$NR^5R^6$ | H | Me | H | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 585 | Me | 6-$NR^5R^6$ | H | CO Me | H | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 586 | Me | 6-$NR^5R^6$ | H | $CO_2$tBu | H | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 587 | Me | 6-$NR^5R^6$ | H | H | H | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 588 | Me | 6-$NR^5R^6$ | H | piperazine | | / | $C_2$ | 4-piperazine-1-yl | 1-Naphthalin | |
| 589 | Me | 6-$NR^5R^6$ | H | Me | H | / | $C_3$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 590 | Me | 6-$NR^5R^6$ | H | CO Ph | H | / | $C_3$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 591 | Me | 6-$NR^5R^6$ | H | CO Me | H | / | $C_3$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 592 | Me | 6-$NR^5R^6$ | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 593 | Me | 6-Pyrrol | H | / | / | / | $C_3$ | 4-Piperidin-1-yl | 5-Tetralin | |
| 594 | Et | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe-Ph | |
| 595 | Et | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-pyrimidine | |

| No | $R^1/R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | A | B | Ar | |
|---|---|---|---|---|---|---|---|---|---|---|
| 596 | Et | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-OMe-1-Naphtha-lin | |
| 597 | Et | H | H | / | / | / | $C_2$ | 4-piperazine-1-yl | 2-Me,3-Me-Ph | |

These compounds are suitable for the treatment of mood disorders caused by the central nervous system, such as seasonal affective disorders and dysthymia. These also include anxieties, such as generalized anxiety disorder, panic attacks, sociophobia, compulsive neuroses and post-traumatic stress symptoms, memory disorders including dementia, amnesia and senile dementia, and also psychogenic eating disorders, such as anorexia nervosa and bulimia nervosa.

It has now been found that compounds of the formula I



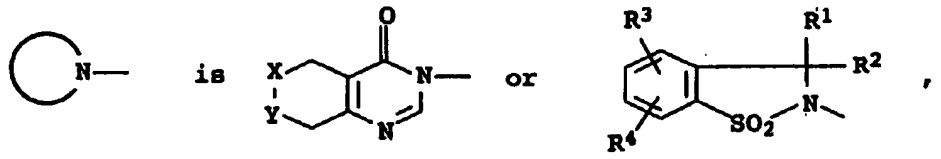
(I),

in which

A is branched or unbranched ($C_{1-10}$)-alkylene or straight-chain or branched ($C_{2-10}$)-alkylene which comprises at least one group Z selected from the group consisting of O, S, $NR^8$, cyclopropyl, $CO_2$, CHOH, a double and a triple bond,

B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine or the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by ($C_{1-6}$)-alkyl, branched or unbranched, O-($C_{1-6}$)-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, $NR^2_2$, $CO_2R^2$, cyano or phenyl, is tetraline, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by ($C_{1-4}$)-alkyl or O-($C_{1-4}$)-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from the group consisting of O and N, and which may be fused with other aromatic radicals,



one of the two radicals X, Y being $CH_2$ and the other being $NR^9$,

$R^1$, $R^2$ independently of one another are $C_1$-$C_6$-alkyl,

$R^3$, $R^4$ independently of one another are hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, OH, O-$(C_{1-6})$-alkyl, branched or unbranched, F, Cl, Br, I, trifluoromethyl, $NR^5R^6$, $CO_2R^7$, nitro, cyano, pyrrole, are a phenyl-$C_1$-$C_4$-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

$R^5$, $R^6$ independently of one another are hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, COPh, $CO_2$tBu, CO-$(C_{1-4})$-alkyl or together are a 5- or 6-membered ring which may contain a second nitrogen (for example piperazine),

$R^7$ is hydrogen or $(C_{1-6})$-alkyl, branched or unbranched,

$R^8$ is hydrogen or $C_1$-$C_4$-alkyl,

$R^9$ is hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, CO-$(C_{1-4})$-alkyl, $CO_2$tBu, CO-aryl or a phenyl-$C_1$-$C_4$-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

and salts thereof,

are suitable for preparing medicaments for the prophylaxis and therapy of neurodegeneration, cerebral trauma and cerebral ischemia, in particular stroke, and of diseases which are caused by these disorders.

A use according to the invention also relates to neuroprotection.

The preparation of these pyrimidine derivatives is described in the patents mentioned at the outset.

The preparation as a medicament is carried out using a compound of the formula I or its pharmacologically acceptable acid addition salt as active compound, together with customary excipients and diluents.

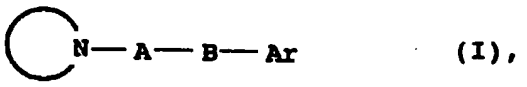
The use according to the invention can be carried out in a customary manner, orally or parenterally, intravenously or intramuscularly.

The dosage depends on the age, on the state and the weight of the patient and on the type of administration. In general, the daily dose of active compound is between approximately 1 and 100 mg/kg of body weight in the case of oral administration and between 0.1 and 10 mg/kg of body weight in the case of parenteral administration.

The medicaments can be used in solid or liquid form in customary pharmaceutical administration forms, for example as tablets, film-coated tablets, capsules, powders, granules, sugar-coated tablets, suppositories, solutions, ointments, creams or sprays. These are prepared in a customary manner. Here, the active compounds can be processed with the customary pharmaceutical auxiliaries, such as tablet binders, fillers, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, sustained-release agents, antioxidants and/or propellants (cf. H. Sucker et al.: Pharmazeutische Technologie [Pharmaceutical Technology], Thieme-Verlag, Stuttgart, 1978). The resulting administration forms generally comprise the active compound in an amount of from 1 to 99% by weight.

We claim:

1. The use of compounds of the formula I



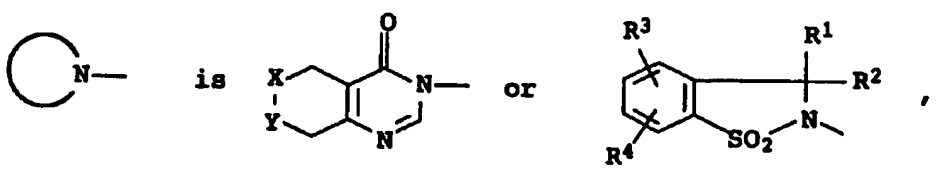
(I),

in which

A is branched or unbranched ($C_{1-10}$)-alkylene or straight-chain or branched ($C_{2-10}$)-alkylene which comprises at least one group Z selected from the group consisting of O, S, $NR^6$, cyclopropyl, $CO_2$, CHOH, a double and a triple bond,

B is 4-piperidine, 4-tetrahydro-1,2,3,6-pyridine, 4-piperazine or the corresponding cyclic compounds which are enlarged by a methylene group, where A is attached via a nitrogen atom of B and

Ar is phenyl which is unsubstituted or substituted by ($C_{1-6}$)-alkyl, branched or unbranched, O-($C_{1-6}$)-alkyl, branched or unbranched, OH, F, Cl, Br, I, trifluoromethyl, $NR^2_2$, $CO_2R^2$, cyano or phenyl, is tetralin, indane, a higher fused aromatic, such as naphthalene, which is unsubstituted or substituted by ($C_{1-4}$)-alkyl or O-($C_{1-4}$)-alkyl, is anthracene or a 5- or 6-membered aromatic heterocycle having 1 or 2 hetero atoms which, independently of one another, are selected from the group consisting of O and N, and which may be fused with other aromatic radicals,



one of the two radicals X, Y being $CH_2$ and the other being $NR^9$,

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$R^1$, $R^2$ independently of one another are $C_1$-$C_6$-alkyl,

$R^3$, $R^4$ independently of one another are hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, OH, O-$(C_{1-6})$-alkyl, branched or unbranched, F, Cl, Br, I, trifluoromethyl, $NR^5R^6$, $CO_2R^7$, nitro, cyano, pyrrole, are a phenyl-$C_1$-$C_4$-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

$R^5$, $R^6$ independently of one another are hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, COPh, $CO_2$tBu, CO-$(C_{1-4})$-alkyl or together are a 5- or 6-membered ring which may contain a second nitrogen (for example piperazine),

$R^7$ is hydrogen or $(C_{1-6})$-alkyl, branched or unbranched,

$R^8$ is hydrogen or $C_1$-$C_4$-alkyl,

$R^9$ is hydrogen, $(C_{1-6})$-alkyl, branched or unbranched, CO-$(C_{1-4})$-alkyl, $CO_2$tBu, CO-aryl or a phenyl-$C_1$-$C_4$-alkyl radical which for its part may be substituted on the aromatic ring by F, Cl, Br, I, $C_1$-$C_4$-alkyl, $C_1$-$C_4$-alkoxy, trifluoromethyl, hydroxyl, amino, cyano or nitro,

and their salts with pharmacologically acceptable acids for preparing medicaments for the prophylaxis and therapy of cerebral ischemia and stroke.